"ROLE OF LEUKOCYTE COUNT, NEUTROPHIL-LYMPHOCYTE RATIO AND PLATELET-LYMPHOCYTE RATIO AS A PROGNOSTIC MARKER IN PESTICIDE POISONING."

By

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BLDE (DEEMED TO BE) University, Vijayapura, Karnataka

In partial fulfillment of the requirements for the award of the degree of

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IN

PATHOLOGY

Under the Guidance of

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ABSTRACT

Introduction-

Pesticides are chemical compounds used for crop protection from rodents and insects. As useful as they can be, poisoning with them is a very common occurrence in farmers. Therefore these are known as HHP (Highly hazardous pesticides) by WHO. In an emergency setting, the identification of quick and powerful prognostic markers can be of high significance in the management of these pesticide poisoning patients.

Aims and Objectives-

To assess the severity of Pesticide Poisoning by assessing the leukocyte count, neutrophil count, neutrophil-lymphocyte ratio and platelet-lymphocyte ratio and its comparison with levels of Plasma Cholinesterase as an aid to clinical diagnosis, for early treatment of the patients.

Materials and methods-

A cross sectional study was done on 148 confirmed cases of pesticide poisoning admitted to the casualty in the period of 1.5 years (1st November 2018 - 30th May 2020). Blood samples were collected in EDTA and plain tubes within 24 hours of admission and the values of total leukocyte Count (TLC), neutrophil count, neutrophil-lymphocyte ratio, platelet-lymphocyte ratio and plasma cholinesterase (PChE) were measured and compared. The severity of poisoning was assessed according to Peradeniya Organophosphorus (POP) scale.

Results-

Majority of the patients were between 21-30 years. 67 (45.3%) were males and 81 (54.7%) were females. Approximately 89.86% (133 cases) of the poisoning cases were due to Organophosphorus compounds and remaining 10.14% (15 cases) were due to carbamate poisoning. The severely poisoned patients according to POP scale had more leukocyte count,

neutrophil count, neutrophil-lymphocyte ratio and platelet lymphocyte ratio; and less plasma cholinesterase level as compared to the patients with mild and moderate poisoning.

Conclusion-

Total Leukocyte count, neutrophil count, neutrophil-lymphocyte ratio and platelet lymphocyte ratio are simple and easy to use parameters for estimating the severity of pesticide poisoning and assessing its prognosis.

Keywords-

Pesticide poisoning, Neutrophil-lymphocyte ratio, Platelet lymphocyte ratio, Plasma cholinesterase, Total Leukocyte count.

LIST OF ABBREVATIONS USED

CBC	**Complete Blood Count**
DDT	**Dichlorodiphenyltrichloroethane**
EPN	**O-ethyl O-(4 nitrophenyl) phenylphosphonothioate**
NCRB	**National Crime Records Bureau**
Co A	**Coenzyme A**
VAchT	**Vesicular Acetylcholine transporter**
PMN	**Polymorphonuclear neutrophils**
NET	**Neutrophil Extracellular traps**
ICU	**Intensive Care Unit**
ED	**Emergency Department**
NLR	**Neutrophil to lymphocyte ratio**
PLR	**Platelet to lymphocyte ratio**
POP	**Peradeniya Organophosphorus Poisoning scale**
GCS	**Glassgow Coma Scale**
PSS	**Poisoning Severity Scale**
SOFA	**Severe Organ Failure Assessment**
TLC	**Total Leukocyte Count**
ALC	**Absolute Leukocyte Count**
PQ	**Paraquat**
OP	**Organophosphorus**

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INTRODUCTION

Pesticides are chemical compounds very commonly used in farming for crop protection and pest control. Their widespread use and over the counter availability have increased the risk of poisoning with these compounds, thereby making them one of the leading causes of accidental and suicidal poisoning in India. Annually, approximately 2,50,000–3,00,000 deaths occur due to pesticide poisoning worldwide.[1] The effective number of cases of pesticide poisoning occurring in India annually has been estimated by G. Ravi et al in 2007 to be up to 76000, much higher than the figure of NCRB (National Crime Records Bureau)[2] and it has been reported that 70% of pesticide poisonings are suicidal.[1] Several studies undertaken in India have revealed the incidence of suicides due to poisoning to vary from 8 to 43 per 1,00,000 population with a pronounced State-to-State variation, the highest being in Kerala while the lowest is in Manipur.[3]

Dundar ZD, Ergin M, Koylu R, Ozer R, Cander B and Gunaydin YK in their study found that the more severely poisoned patients had leukocytosis, neutrophilia and lymphocytopenia within the first 24 h after admission to the Emergency Department (ED).[1]

Oxidative stress is the major mechanism in the pathophysiology of most toxins and diseases.[4] Experimental and clinical studies have reported that the production of free radicals is increased in pesticide poisoning. More severe pesticide poisonings will lead to an increased production of free radicals. When the production of free radicals exceeds the antioxidant capacity of the patient, there will be noticeable changes on the CBC due to the oxidative stress. Leukocytosis, neutrophilia, lymphocytopenia and monocytosis can be detected on CBC in the acute period of the clinical course when the oxidative stress is increased.[1] Leukocytosis in

stress like poisoning is due to neutrophilia caused by neutrophil margination, and not due to increased marrow production. Neutrophils are produced in the bone marrow and comprise approximately 65% of the peripheral blood. These cells are critically important to generate an immune response and migrate from the blood to the tissues during any stress like infection or poisoning. Therefore, patients with significant stress should have a higher degree of leukocytosis compared to patients with minor or no stress.[5]

As reported in experimental and clinical studies, leukocytosis and neutrophilia can be seen in the early stages of pesticide poisoning, and leukopenia and lymphocytopenia develop in the later stages. [1] But in this condition, the complete blood count (CBC) is of value only when there is a clinical history of pesticide abuse. Particularly in the absence of witnesses, it becomes impossible to identify when, how much, and to which pesticides the patient was exposed. In such cases, the severity of poisoning should be evaluated by objective criteria on admission to the Emergency Department (ED). [1]

In addition to this, at a primary setup, where the measurement of cholinesterase activity cannot be done, management is solely based on the assessment of severity of intoxication, which depends on clinical findings and basic blood parameters. In conditions like poisoning, leukocytosis is a very common finding, and the white blood cell count returns to normal level after treatment.[5]

Goodman and colleagues in their study showed that neutrophil-lymphocyte ratio is a more sensitive marker than leukocyte counts alone in prediction of acute inflammatory conditions like appendicitis.[6] Neutrophil to Lymphocyte ratio can also be used in cases of acute pesticide exposure as the bodily reaction towards the pesticide starts with an acute inflammatory response.

Vijayapura district is one of the economically challenged districts of Northern part of state of Karnataka and also a drought prone area, making it a deadly combination where suicides due to pesticide poisoning are on the rise. Hence, this study aims to help in correlation of the severity of poisoning with neutrophil count, neutrophil-lymphocyte ratio and platelet-lymphocyte ratio and will also help to assess the prognosis.

AIMS AND OBJECTIVES

To assess the severity of Pesticide Poisoning by assessing the leukocyte count, neutrophil-lymphocyte ratio and platelet-lymphocyte ratio and its comparison with levels of Plasma Cholinesterase as an aid to clinical diagnosis, for early treatment of the patients.

REVIEW OF LITERATURE

Pesticides are poisonous chemicals intended for preventing, destroying or controlling any pest, including vectors of human and animal disease, unwanted species of plants or animals causing harm during the production, processing, storage, transport or marketing of food, agricultural commodities, wood or animal feedstuffs.[7] They are mainly used in agriculture and horticulture but also in households, as well as in health campaigns e.g. to eradicate vector borne diseases such as yellow fever and malaria.

History of pesticides:

In the 1800s, chemists synthesized the first organophosphorus chemical. Researchers later created various forms of the organophosphate and applied the chemicals as insecticides. In the 1930s, a German chemist developed exceptionally lethal organophosphates, which were soon applied to weapon systems and were used in World War II (1939-1945). These compounds were eventually classified as the first nerve agents. Continued investigation of these chemicals over the past seventy years has produced greater variants of organophosphorus insecticides and nerve agents.[8,9]

In 1994, Aum Supreme Truth, a religious cult, synthesized sarin and employed the chemical against Japanese government agencies and citizens to further the cult's political and religious goals. The terrorist cult released 12 liters of a 70% sarin solution in Matsumoto, Japan. The nerve agent killed 7 people and caused 56 hospital inpatient casualties, 208 hospital outpatient casualties, and 277 on-scene treated sicknesses. In 1995, the terrorist group again released sarin, this time on the Tokyo subway, killing 12 people and causing over 500 illnesses, which included 100

first care responders.[10]

Sarin, soman, tabun, and VX are the most common nerve agents. Despite being first developed in the 1930s, it was not until the 1980s, that the first employment of nerve agents as a weapon was documented. Iraq employed tabun and sarin against Iranian military forces between 1983 and 1984 and between 1987 and 1988 during the Iran-Iraq War. Iraq also employed sarin against civilian Iraqi Kurds, an ethnic sub-population of Iraq, between 1987 and 1988.[8]

Classification of Pesticides:[7,11]

Pesticides are classified by

1) Their chemical class- organochlorines, organophosphates, carbamates, etc.

2) Their function- insecticides, fungicides, herbicides or rodenticides

3) By hazard in the toxicological classes

Class Ia- extremely hazardous

Class Ib- highly hazardous

Class II- moderately hazardous

Class III- slightly hazardous

U- active ingredients unlikely to present any harm in normal use

O- obsolete.

Table 1: Classification of pesticides according to chemical class

Organochlorine compounds	Organophosphorus compounds	Carbamates
Methoxychlor	Chlorthion	Carbaryl
DDT [Dichlorodiphenyltrichloroe--thane]	Diazinon	Pyrolan
HCH [Hexachlorocyclohexane]	Dioxathion	Dimetilan
Chlordene	Dimethoate	Propoxur
Hepatochlor	EPN [O-ethyl O-(4 nitrophenyl) phenylphosphonothioate]	Synthetic
Dieldrin	Malathion	Pyrethroids
Aldrin	Fenthion	
	Methylparathion	
	Parathion	
	Ronnel	
	Trichlorfos	
	Dichlorvos Chlorpyrifos	

PHARMACOLOGY & PATHOPHYSIOLOGY OF ORGANOPHOSPHORUS COMPOUNDS

Organophosphates are volatile liquid chemicals characterized by central phosphorous atom bound to an oxygen atom, two alkyl groups, and a leaving group (Figure 1). The most likely human exposure to organophosphates is through inhalation, apart from the other routes such as transconjunctival, transdermal or ingestion. Rare reports of intramuscular, intravenous and subcutaneous toxicity of organophosphorous compounds are available where the onset of symptoms would be delayed and persist for a longer duration of antidote therapy.[9]

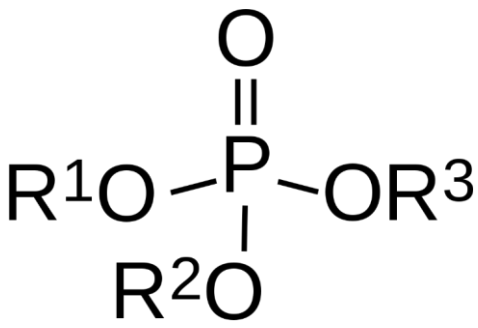


Figure 1: Chemical structure of Organophosphorus Compound
R- Alkyl group

The cholinergic system:

The preganglionic fibres terminating in the adrenal medulla, the autonomic ganglia (both parasympathetic and sympathetic) and the post ganglionic fibres of the parasympathetic division use acetylcholine as a neurotransmitter.[12]

Acetylcholine:

Acetylcholine is the acetyl ester of choline which exists enclosed in small, clear synaptic vesicles in the terminal buttons of neurons in high concentration that release acetylcholine (Cholinergic neurons).[12]

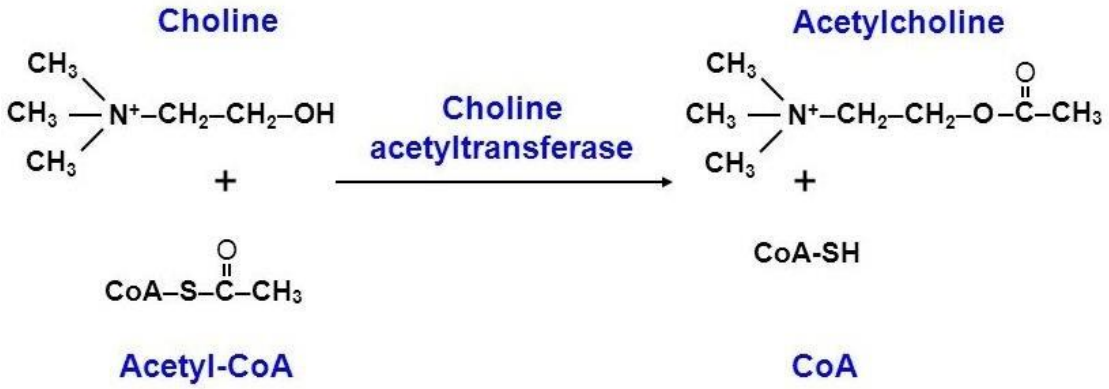


Figure 2: Formation of acetylcholine

Synthesis of acetylcholine involves the reaction of choline with acetate. Choline is an important amine synthesized in neurons and is the precursor of the membrane phospholipids namely phosphatidylcholine and spingomyeline and also the precursor of the signalling phospholipids i.e. platelet-activating factor and sphingosyl phosphorylcholine. There is an active uptake of choline via a transporter into cholinergic neurons.[12]

The acetate is activated by combination of acetate groups with reduced co-enzyme A. The reaction between active acetate (acetyl co-enzyme A, acetyl- COA) and choline is catalyzed by the enzyme choline acetyl transferase present in the axoplasm (Figure 2). The enzyme is found in high concentration in the cytoplasm of cholinergic nerve endings. Acetylcholine is then taken up into synaptic vesicles by a transporter on the vesicular membrane called Vesicular Acetylcholine transporter (VAchT).[12]

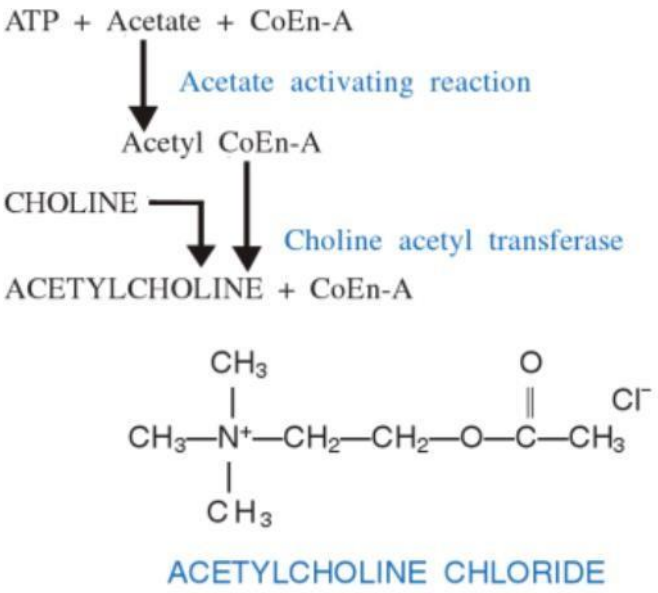


Figure 2.1: Formation of Acetylcholine

Cholinesterase:

Acetylcholine is removed from the synapse by hydrolysis of acetylcholine to choline and acetate, a reaction catalyzed by the enzyme acetyl cholinesterase (Figure 3). This enzyme is called true or specific cholinesterase. Its greatest affinity is for acetylcholine, but it also hydrolyzes other choline esters. Out of the various esterases present in the body; one esterase found in plasma is capable of hydrolyzing acetylcholine but has different properties from acetylcholinesterase. It is therefore called pseudo cholinesterase or non-specific cholinesterase.[13]

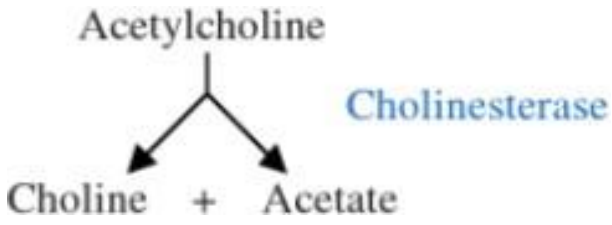


Figure 3: Hydrolysis of acetylcholine by cholinesterase

Acetylcholine receptors:

Two families of acetylcholine receptors designated as muscarinic and nicotinic receptors can be distinguished from each other on the basis of their different affinities for agents that mimic the action of acetylcholine. Muscarinic receptors are G-protein coupled receptors whereas nicotinic receptors are ligand gated cation channels.[12]

1. Muscarinic receptors (M_1,M_2,M_3,M_4 and M_5)

These receptors have been found on ganglia of the peripheral nervous system and on the autonomic effector organs, such as heart, smooth muscle, brain and exocrine glands. Specifically, although all five subtypes have been found on neurons, M1 receptors are also found in gastric parietal cells, M2 receptors on cardiac cells and smooth muscle, and M3 receptors on exocrine glands and smooth muscle. M4 and M5 receptors are present in the nerve endings of certain areas of brain and regulate other neurotransmitters.[12]

2. Nicotinic receptors (N_N and N_M)

Nicotinic receptors are located in the CNS, adrenal medullary cells, autonomic ganglia, and the neuromuscular junction. These receptors, in addition to binding acetylcholine, also recognize nicotine but show only a week affinity for muscarine. Nicotine initially stimulates and then blocks the receptors.[12]

MODE OF ACTION

When pesticides like organophosphates enter the body, acetylcholine esterases are bound to organophosphates. Acetylcholine molecules are not hydrolyzed and thus accumulate in the synapse and cause over-stimulation of the nervous system. This over-stimulation leads to a variety of physiological effects, which are dependent on the type of neural receptor and location in the body.[9]

In the peripheral nervous system (PNS), over stimulation of muscarinic receptors causes continuous contraction of smooth muscles and secretion of exocrine glands. Effects include "miosis with dim or blurred vision, eye pain (ciliary spasm) or headache, tearing, rhinorrhea, salivation, bronchoconstriction and excessive bronchosecretions with dyspnea, bradyarrhythmias, hypotension, nausea and vomiting, abdominal cramps, diarrhea and bowel incontinence, and urinary incontinence". Also in the PNS, organophosphates lead to the over- stimulation of nicotinic receptors causing uncontrolled contraction of voluntary muscles.[9]

Both muscarinic and nicotinic receptors are found in the central nervous system (CNS). In the CNS, over- stimulation of both receptor types causes "mild to severe behavioral and cognitive changes, impaired consciousness or coma, seizures, or central apnea."[7] If the exposed person survives the initial effects of organophosphate poisoning, other symptoms may persist for weeks and include "irritability, anxiety, depression, fatigue, insomnia, nightmares, and impaired judgment".[9,14]

CLINICAL MANIFESTATIONS OF ORGANOPHOSPHORUS POISONING:

Organophosphorus compounds are irreversible anticholinesterases and cause signs and symptoms of cholinergic excess.

Main actions/effects:

1. Muscarinic or hollow organ parasympathetic manifestations.
2. Nicotinic or autonomic ganglionic and somatic (NMJ) effects
3. Central nervous system (CNS) effects

1. **Muscarinic effects:** [15,16,17,18]

- Bronchial tree: Tightness in chest, rhinitis, dyspnoea, cough, wheezing suggestive of bronchoconstriction, increased bronchial secretions, pulmonary edema, cyanosis.
- Gastrointestinal tract: Nausea, vomiting, cramps, diarrhea, tenesmus, faecal incontinence
- Sweat gland: Increased sweating
- Salivary gland: Increased salivation
- Lacrimal gland: Increased lacrimation
- Cardiovascular system: Ventricular fibrillation and ventricular tachycardia
- Pupils: Miosis
- Ciliary body: Blurring of vision
- Bladder: Frequency / urinary incontinence

2. **Nicotinic Effects:** [15,16,17,18]

- Striated muscles– Muscular twitching, fasciculation, weakness, cramps and paresis including that of muscles of respiration
- Sympathetic ganglia – pallor, tachycardia, increased BP.

3. **Central Nervous system:** [15,16,17,18,19]

- Giddiness, tension, anxiety, restlessness, emotional lability, excessive dreaming, insomnia, headache, tremor, depression, drowsiness, confusion, slurred speech.
- Generalized weakness, coma with absence of reflexes, type I paralysis, convulsions.

- Cheyne Stokes respiration, depression of respiratory and circulatory centres with dyspnoea, cyanosis and fall in Blood pressure.

INVESTIGATIONS IN ORGANOPHOSPHORUS POISONING:

The role of estimation of serum cholinesterase:[11,16,20]

Estimation of acetyl cholinesterase level in circulation is theoretically preferred in organophosphorus poisoning since it would reflect the degree of inhibition of synaptic cholinesterase at motor end plates. But, in practice, estimation of plasma cholinesterase has an advantage because the measurement is simpler and more accurate than estimation of the acetylcholinesterase. Plasma cholinesterase levels can indicate the prior presence of cholinesterase inhibition even after recovery of acetylcholinesterase activity by pralidoxime in organophosphorus poisoning.

In acute poisoning, manifestations generally occur only after more than 50% of cholinesterase is inhibited. The normal values range between 5000 to 12000 U/L. According to Proudfoot, the Organophosphorus poisoning may be classified based on the levels of plasma cholinesterase on presentation as follows:[21]

Table 2: Cholinesterase levels according to the severity of poisoning

Poisoning	**Pl. Cholinesterase level**
Mild	20-50% of normal
Moderate	10-20% of normal
Severe	<10% of normal

Changes in acetylcholine levels during poisoning and treatment[16]

Cholinesterase activity of red blood cells is instantly and completely restored and long lasting, but the return of activity of plasma cholinesterase (PChE) is transient and variable after oximes.

Time of ingestion & relation to serum cholinesterase activity: A definite correlation between time of ingestion and serum cholinesterase activity is found viz., longer the interval lower the activity. It appears that in doubtful cases or in cases with bizarre clinical picture, and in cases where more than one poisonous substance is ingested, the estimation of serum cholinesterase activity would be of some importance in the diagnosis of the case. Perhaps individual response to excessive cholinergic activity is very variable at identical levels of serum cholinesterase activity.

Leukocyte count:

Leukocyte count, also known as White blood cell count, is a parameter indicating the stress of infection in a patient. In conditions like infection, there is an increased production of leukocytes from the bone marrow to combat and control the spread of infection to other parts of the body. However, leukocytosis in stress like poisoning is due to neutrophilia caused by neutrophil margination, and not due to increased marrow production.[5]

Neutrophils:

Neutrophils, also known as polymorphonuclear (PMN) leukocytes, are the most abundant cell type in human blood. They are produced in the bone marrow in large numbers, $\sim 10^{11}$ cell per day. Under homeostatic conditions, neutrophils enter the circulation, migrate to tissues, where they complete their functions, and finally are

eliminated by macrophages, all in the lapse of a day.[22]

Three main antimicrobial functions are recognized for neutrophils: phagocytosis, degranulation, and the release of nuclear material in the form of neutrophil extracellular traps (NETs).[22]

Neutrophils travel via the blood stream in a laminar flow. But, in stressful bodily conditions conditions like poisoning or sepsis, they migrate to the periphery of the blood vessel. Hence, on performing a phlebotomy, neutrophil counts are acutely raised in the blood. Also, the bone marrow responds to stress by increasing the production of neutrophils and circulating them in the blood. Thus, in a patient of poisoning, neutrophils are acutely raised in complete blood count.

It is also noted in other studies that as the patient recovers, there is a fall in the values of neutrophil count.[1,5]

Neutrophil lymphocyte ratio:

The physiological immune response of circulating leukocytes to various stressful events like poisoning, is often characterized by an increase in neutrophil counts and a decline in lymphocyte counts. Zahorec proposed to use the ratio of both as an additional infection marker in clinical ICU practice.[23] This so-called "neutrophil-lymphocyte stress factor" was found to correlate well with the severity of disease and outcome, according to Acute Physiology and Chronic Health Evaluation II (APACHE- II) and Sepsis-related Organ Failure Assessment (SOFA) scores.[23,24,25] Earlier, Goodman and colleagues had already shown that a so-called neutrophil:lymphocyte ratio provided a more sensitive parameter than the leucocyte count in the prediction of appendicitis.[6] Recently, Walsh and colleagues used a similar ratio - referred to as the neutrophil-to-lymphocyte ratio - as a prognostic factor in the preoperative assessment of patients with colorectal cancer.[26] In this setting, an

increased neutrophil-to-lymphocyte ratio correlated with overall and cancer-specific survival. Currently, both lymphocytopenia and the neutrophil lymphocyte count ratio (NLCR), as we refer to it, are gaining interest as independent predictors of survival in various clinical circumstances ranging from pesticide poisoning to oncological conditions to patients with cardiovascular diseases.[27,28]

Platelet lymphocyte ratio:

Platelets are rich in proinflammatory agents and they release highly active microparticles in the proinflammatory states.

Over the past decade, PLR has emerged as an informative universal laboratory marker for predicting various prothrombotic, neoplastic, and metabolic diseases. PLR fluctuations can be interpreted in the context of the underlying multifaceted immune-inflammatory reactions. The value of PLR as an inflammatory marker increases when its fluctuations are interpreted along with other complementary hematologic indices, particularly the neutrophil-to-lymphocyte ratio (NLR), which provides additional information about the disease activity, presence of neutrophilic inflammation, infectious complications, and severe organ damage in systemic lupus erythematosus. PLR better predicts clinical outcomes in patients with systemic inflammation than either platelet or lymphocyte count.[29]

Basically, the magnitude of stress-induced hypercortisolemia with subsequent release of platelets into the bloodstream and transient lymphopenia influence the degree of elevation of PLR across numerous proinflammatory and prothrombotic disease states.[29]

However, a retrospective study done by Wang WJ et al indicates that platelet lymphocyte ratio is not a useful predictor for acutely poisoned patients, specifically paraquat poisoning.[30]

Clinical scales for measuring the severity of poisoning:

Few clinically assessed parameters are combined and used to measure the severity of poisoning. These are as follows:

1. Peradeniya Organophosphorus Poisoning (POP) scale (Table 2)
2. Glasgow Coma Scale (GCS) (Table 6)
3. Poisoning Severity Score (PSS): The Poisoning Severity Score grades severity as (0) none, (1) minor, (2) moderate, (3) severe, and (4) fatal poisoning.
4. SOFA (Sequential Organ Failure Assessment) score (Table 8)

According to the study conducted by Raveendra K, Mohan C, Kodur N [31], any of the above scales can be used to measure the severity of Organophosphorus poisoning.

Peradeniya organophophorus poisoning (POP) scale:

Peradeniya Organophosphorus poisoning scale (Peradeniya referring to suburb of the city of Kandy, Sri Lanka) is a clinical scale developed by Senanayake et al at the university of Peradeniya, Srilanka to assess the severity of OP intoxication.

Peradeniya OP poisoning scale is a simple and effective system to determine the severity of organophosphorus poisoning. The score is obtained at initial presentation before doing any medical intervention and it represents the muscarinic, nicotinic and central effects of acute cholinergic manifestations of OP poisoning.[32]

Table 3: Peradeniya Organophosphorus Poisoning (POP) Scale. [32]

Sr. No.	Parameter	Score
1.	**Miosis**	
	- Pupil size >2mm	0
	- Pupil size ≤2mm	1
	- Pupils pin point	2
2.	**Fasciculations**	
	- None	0
	- Present but not generalized or continuous	1
	- Generalized and continuous with central cyanosis	2
3.	**Respiration**	
	- Respiratory rate ≤20/min	0
	- Respiratory rate >20/min	1
	- Respiratory rate >20/min with central cyanosis	2
4.	**Bradycardia**	
	- Pulse rate >60/min	0
	- Pulse rate 41-60/min	1
	- Pulse rate ≤40/min	2
5.	**Level of consciousness**	
	- Conscious and rational	0
	- Impaired, responds to verbal commands	1
	- Impaired, no response to verbal commands	2
	(if convulsion present add 1)	
	Total	11

Table 4: POP Scoring [32]

Grade	Score
Mild	<4
Moderate	4-7
Severe	>7

Table 5: Relation of Grade of poisoning to cholinesterase activity:[33]

Grade of poisoning	Cholinesterase activity
Mild	20-50%
Moderate	10-20%
Severe	<10% (less than 10%)

Table 6: Glasgow coma scale (GCS)[34]

Sr. No.	Parameter	Score
1.	**Eye:**	
	Does not open eyes	1
	Opens eyes in response to pain	2
	Opens eyes in response to voice	3
	Opens eyes spontaneously	4
2.	**Verbal:**	
	Makes no sounds	1
	Makes sounds	2
	Words	3
	Confused, disoriented	4
	Oriented, converses normally	5
3.	**Motor:**	
	Makes no movements	1
	Extension to painful movement (decerebrate response)	2
	Abnormal flexion to painful response (decorticate response)	3
	Flexion / Withdrawal to painful stimuli	4
	Localizes to painful stimuli	5
	Obeys commands	6

Table 7: GCS scoring [34]

Grade	GCS scoring
Minor	>13
Moderate	8-13
Severe	<8

SOFA score:[25]

Table 8: SOFA score

Sr. No.	Parameter	Score
1.	**Respiratory system:**	
	PaO_2/FiO_2 [mmHg (kPa)]	
	a. ≥ 400 (53.3)	0
	b. < 400 (53.3)	+1
	c. < 300 (40)	+2
	d. < 200 (26.7) and mechanically ventilated	+3
	e. < 100 (13.3) and mechanically ventilated	+4
2.	**Nervous system:**	
	Glasgow coma scale	
	a. 15	0
	b. 13-14	+1
	c. 10-12	+2
	d. 6-9	+3
	e. <6	+4
3.	**Cardiovascular system:**	
	Mean arterial pressure OR administration of vasopressors required	
	a. MAP ≥ 70 mmHg	0
	b. MAP < 70 mmHg	+1
	c. Dopamine ≤5 μg/kg/min or Dobutamine (any dose)	+2
	d. dopamine > 5 μg/kg/min OR epinephrine ≤ 0.1 μg/kg/min OR norepinephrine ≤ 0.1 μg/kg/min	+3
	e. dopamine > 15 μg/kg/min OR epinephrine >0.1 μg/kg/min OR norepinephrine >0.1 μg/kg/min	+4

4.	**Liver:** **Bilirubin (mg/dl) [µmol/L]** a. < 1.2 [< 20] b. 1.2–1.9 [20-32] c. 2.0–5.9 [33-101] d. 6.0–11.9 [102-204] e. > 12.0 [> 204]	 0 +1 +2 +3 +4
5.	**Coagulation:** **Platelets×10^3/µl** a. ≥ 150 b. < 150 c. < 100 d. < 50 e. < 20	 0 +1 +2 +3 +4
6.	**Kidneys:** **Creatinine (mg/dl) [µmol/L] (or urine output)** a. < 1.2 [< 110] b. 1.2–1.9 [110-170] c. 2.0–3.4 [171-299] d. 3.5–4.9 [300-440] (or < 500 ml/d) e. > 5.0 [> 440] (or < 200 ml/d)	 0 +1 +2 +3 +4

Table 9: SOFA score interpretation:[25]

Total SOFA score- 0 to 24

Mortality	**Total score**
<10%	0-6
15-20%	7-9
40-50%	10-12
50-60%	13-14
>80%	15
>90%	16-24

MANAGEMENT OF ACUTE ORGANOPHOSPHORUS POISONING [11,16]

1. Supportive measures:

   Oral suction of secretions

   Maintenance of circulation

   Establishment of respiration

2. Prevention of absorption:

   Decontamination

   Emesis

   Adsorbant

   Cathartics

   Bowel wash

3. Specific chemotherapy:

   Atropine

   Oximes

   Treatment of complications

1. Supportive measures:

It should be ensured that upper airway is not blocked and throat secretions should be intermittently sucked to avoid aspiration. Respiratory insufficiency is the commonest cause of death. Hence, positive pressure ventilation should be given if patient develops signs of respiratory failure.

2. Prevention of absorption:

Decontamination: Contaminated clothing should be changed, skin should be washed.

Emesis: Unless the patient is comatosed, convulsing or has lost the gag reflex emesis should be initiated. Should these contraindications be present, endotracheal intubation should precede gastric lavage with wide bore tube.

Adsorbant: Activated charcoal functions as an adsorbant and should be given within 3 hours of ingestion and if gastric emptying is delayed it may be useful for upto 12 hours after ingestion. It is the most valuable single agent for emergency management of oral drug poisoning.

Cathartics: Cathartics function by decreasing absorption and increasing elimination. It should be administered as early as possible because relapse is thought to be due to delayed absorption.

Bowel wash: To be done twice a day which helps to remove toxic substance from large bowel.

3. Specific therapy:

Atropine:

It is an alkaloid derived from a plant Atropa belladona and Datura stramonium. Atropine acts as a physiological antidote, effectively antagonising the muscarinic receptor- mediated actions of organophosphorus agents. Dose of atropine should be sufficient to produce signs of atropinisation. Size of the pupil is a good indicator for regulating the dose of atropine.

Pharmacological Action: At autonomic ganglia where transmission mainly involves nicotinic receptors, atropine produces partial blockade at high doses. Atropine does not inhibit the nicotinic actions of acetylcholine. To some extent it inhibits the central effects produced by these compounds. Thus, atropine antagonises mainly the muscarinic effects of organophosphorus poisoning. Atropine is partially

detoxified in the liver and partly excreted unchanged in the kidney.

Dosage: In order to prevent pulmonary edema, early prompt atropinisation is important. Severe poisoning may require heavy doses, upto 100 mg over first 24 hours to achieve adequate atropinisation. Atropinisation should be maintained till absorbed organophosphate is fully metabolised which may require 2 - 200 mg or more of atropine over a few hours to several days. Abrupt withdrawal can cause pulmonary edema.

Signs of atropinisation: Pupillary dilatation cannot be taken as an indication of atropinisation since Organophosphorus Compounds can produce both miosis or mydriasis. Pupils becoming initially pinpoint later becoming dilated is a reliable sign of atropinisation. Since tachycardia and bradycardia can occur, tachycardia (130 – 140/min.) cannot be a reliable sign. Other signs include flushing, dry skin and dry mouth. Full atropinisation is indicated by clearing of rales and drying of pulmonary secretions.

Adverse Effects: Dry mouth, hot dry skin, thirst, flushing, fixed dilated pupil, tachycardia, impaired speech, tremor, coma, convulsions, respiratory failure and collapse. Potential fatal dose is 25-30 mg/kg body wt.

Oxime:

Dosage: Pralidoxime- 1gm followed by 500 mg/ 6 hourly for 2 more days.

Obidoxime - 3-6 mg / kg IV over 5-10min.

D.A.M. (Diacetyl Monoxime) -1-2 gm IV slowly.

Pralidoxime chloride is given at a dose of 1gm IV for adults over a period of 15-30 min. A dose of 30 mg/kg IV at a rate not exceeding 500 mg every 4 hours for first 24 hours is also advocated.

MATERIALS AND METHODS

Source of data

The study was done on confirmed cases of Pesticide poisoning who were admitted in the Casualty of BLDE (Deemed to be University) Shri B. M. Patil Medical College, Hospital and Research Centre, Vijayapura. Total 148 patients were included in the study and their hematological and biochemical values were recorded and compared. The hematological and biochemical analysis were done in the Department of Pathology and the Department of Biochemistry, B.L.D.E (Deemed to be University), Shri B. M. Patil Medical College, Hospital and Research Centre, Vijayapura.

Study period: 1st November 2018 - 30th May 2020

Methods of collection of data:

The study included 148 patients clinically diagnosed with pesticide poisoning at the time of admission. The values of total leukocyte Count (TLC), neutrophil count, neutrophil-lymphocyte ratio, platelet-lymphocyte ratio and plasma cholinesterase (PChE) were measured and compared to know the severity of the disease. The values of total leukocyte Count (TLC), neutrophil count and platelet count were measured on Sysmex XN-1000 fully automated hematology analyzer (Figure 4) via hydrodyanamic focusing, forward scatter and side scatter method. Neutrophil-lymphocyte ratio and platelet-lymphocyte ratio were manually calculated. The value of plasma cholinesterase was measured on Ortho Clinical Vitros 250 Chemistry System via Butyrylthiocholine hydrolysis, kinetic assay. (Figure 5)

Figure 4: Sysmex XN 1000 5-part fully automated hematology analyser

Figure 5: Ortho Clinical Vitros 250 Chemistry System

Inclusion criteria

All confirmed cases of pesticide poisoning during study period were included.

Exclusion criteria

Cases of poisoning by unknown compounds and compounds of other chemicals such as benzene, mercury, cadmium etc.

Type of study

Prospective cross-sectional study

STATISTICAL ANALYSIS

All characteristics were summarized descriptively. For continuous variables, the summary statistics of mean± standard deviation (SD) were used. For categorical data, the number and percentage were used in the data summaries and diagrammatic presentation. Chi-square (χ^2) test was used for association between two categorical variables.

The formula for the statistics used is the chi square test which is as given below:

$$\chi_c^2 = \sum \frac{(O_i - E_i)^2}{E_i}$$

The subscript "c" are the degrees of freedom. "O" is observed value and E is expected value. C= (number of rows-1) * (number of columns-1)

The difference of the mean of analysis variables between more than two independent groups was tested by ANOVA test and F test was used for testing of equality of Variance.

ANOVA

Source	d.f.	SS	MS	F
Treatment	$a-1$	SS_{treat}	$\frac{SS_{treat}}{a-1}$	$\frac{MS_{treat}}{MS_{error(a)}}$
Error (a)	$N-a$	$SS_{error(a)}$	$\frac{SS_{error(a)}}{N-a}$	
Time	$t-1$	SS_{time}	$\frac{SS_{time}}{t-1}$	$\frac{MS_{time}}{MS_{error(b)}}$
Treat x Time	$(a-1)(t-1)$	$SS_{treat\ x\ time}$	$\frac{SS_{treat\ x\ time}}{(a-1)(t-1)}$	$\frac{MS_{treat\ x\ time}}{MS_{error(b)}}$
Error (b)	$(N-a)(t-1)$	$SS_{error(b)}$	$\frac{SS_{error(b)}}{(N-a)(t-1)}$	
Total	$Nt-1$	SS_{total}		

The sources of the variation include treatment; Error (a); the effect of Time; the interaction between time and treatment; and Error (b). Error (a) is the effect of subjects within treatments and Error (b) is the individual error in the model. All these add up to the total.

ROC analysis for Sensitivity- specificity was done to check relative efficiency.

sensitivity or true positive rate (TPR)

eqv. with hit rate, recall

$$TPR = TP/P = TP/(TP + FN)$$

specificity (SPC) or true negative rate

$$SPC = TN/N = TN/(FP + TN)$$

precision or positive predictive value (PPV)

$$PPV = TP/(TP + FP)$$

negative predictive value (NPV)

$$NPV = TN/(TN + FN)$$

If the p-value was < 0.05, then the results were considered to be statistically significant otherwise it was considered as not statistically significant. Data were analyzed using SPSS software v.23 (IBM Statistics, Chicago, USA) and Microsoft office.

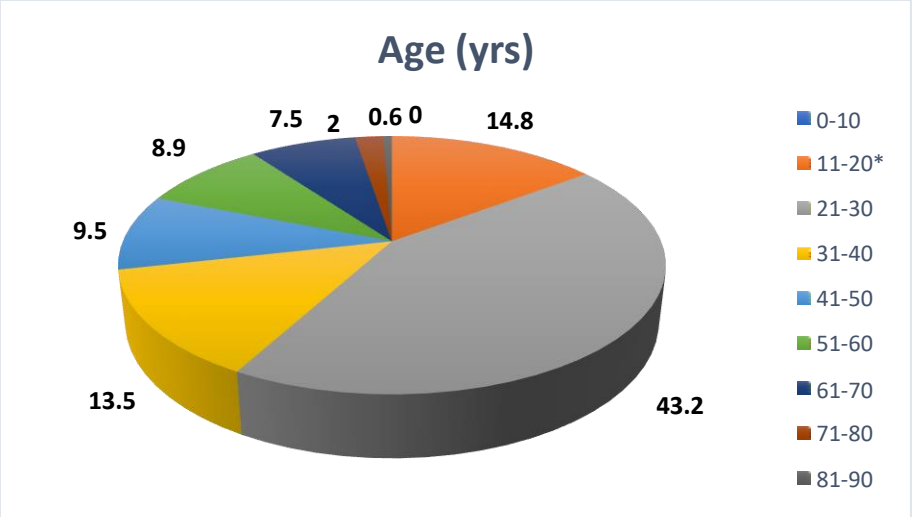
RESULTS

In the present study, out of 148 cases studied, 43.9% cases were of 21-30 years of age group constituting majority of the cases. (Table 10)

Table 10: Distribution of Cases according to Age

Age (yrs)	No	%
0-10	0	0
11-20	22	14.8
21-30	64	43.2
31-40	20	13.5
41-50	14	9.5
51-60	13	8.9
61-70	11	7.5
71-80	3	2.0
80-90	1	0.6
Total	148	100

Figure 6: Distribution of Cases according to Age



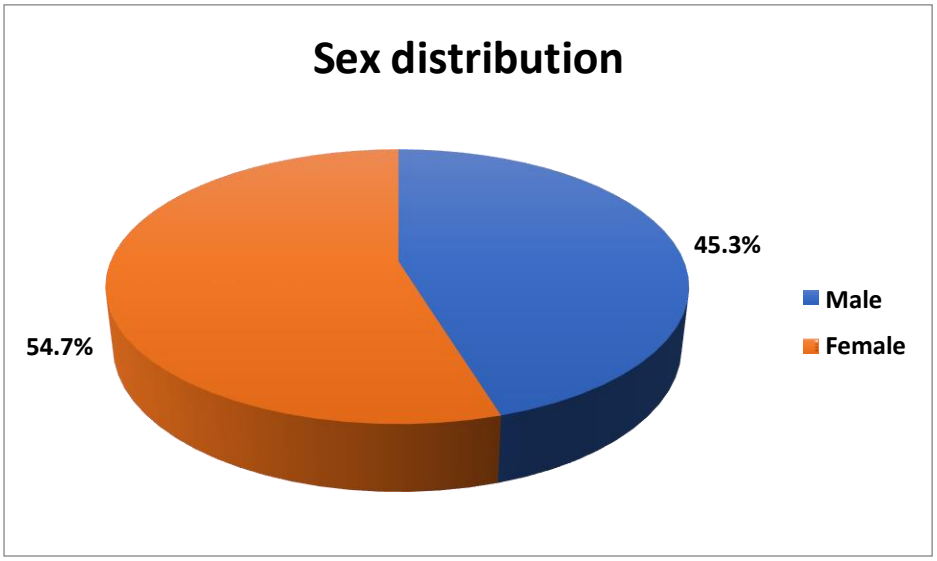
In this study, females constituted 54.7% (81) of the total patients while males constituted 45.3% (67) of the total cases. (Table 11)

Table 11: Distribution of Cases according to Sex

Sex	No	%
Male	67	45.3
Female	81	54.7
Total	148	100

Male to Female Ratio = 1.0:1.2

Figure 7: Distribution of Cases according to Sex



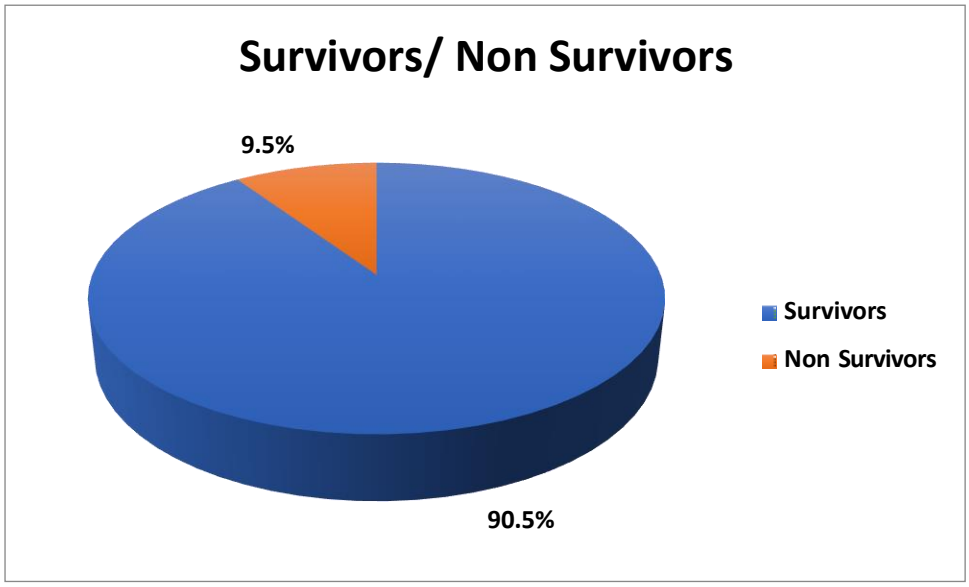
Out of 148 cases, 79.72% (118 cases) of poisoning cases were suicidal, followed by 13.52% (20 cases) of homicidal poisoning. 6.76% (10 cases) of cases were due to accidental consumption of the pesticides. 133 cases (89.86%) of poisoning were due to consumption of Organophosphorus compounds and 15 cases (10.14%) of poisoning were due to carbamate consumption.

Majority of the patients (including those with ventilatory support) survived (90.5%), whereas 9.5% patients succumbed to death, as depicted in table 12 and Figure 8.

Table 12: Distribution of Cases according to Survivors/ Non-Survivors

Survivors/ Non-Survivors	No	%
Survivors	134	90.5
Non-Survivors	14	9.5
Total	148	100

Figure 8: Distribution of Cases according to Survivors/ Non-Survivors

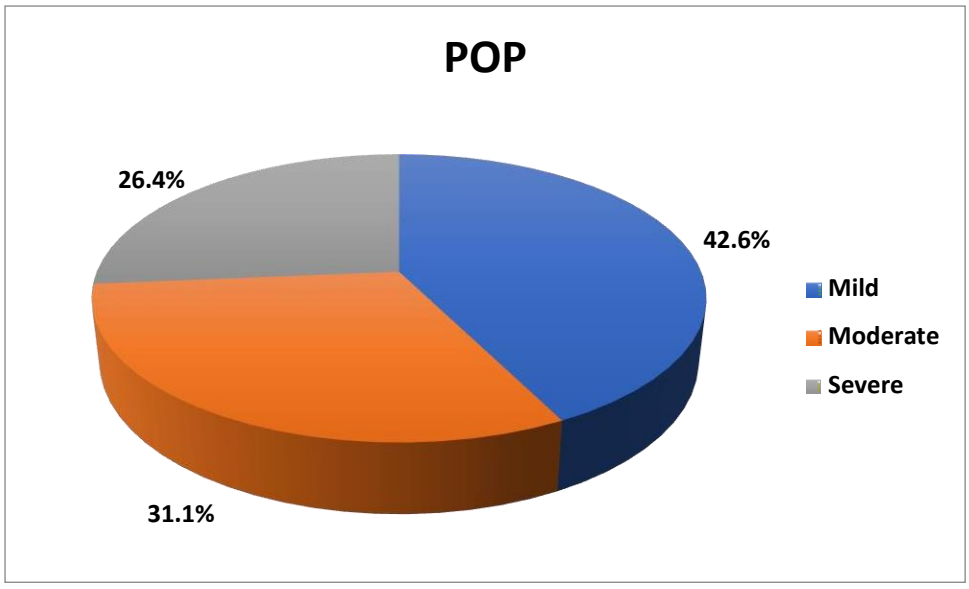


According to POP scale, based on symptoms of poisoning, mild cases comprised 42.6%, moderate cases 31.1% and severe cases 26.4%. (Table 13) (Figure 9)

Table 13: Distribution of Cases according to POP scale

POP	No	%
Mild	63	42.5
Moderate	46	31.1
Severe	39	26.4
Total	148	100

Figure 9: Distribution of Cases according to POP scale



The data and distribution of the measured parameters of collected samples of 148 patients were as follows:

The baseline characteristics of the laboratory parameters are as given in Table 14.

Table 14: Baseline Characteristics of various Laboratory parameters

Descriptive Statistics	Min	Max	Mean	SD
TLC (cells/uL)	1850	39030	13965.5	5843.7
Neutrophils (%)	48	97.1	80.8	10.5
Lymphocytes (%)	1.7	47.2	14.3	9.1
Platelet (cells/uL)	66000	735000	277662.2	106775.5
RDW (%)	12	38.5	15.3	3.2
Plasma Cholinesterase (Units/L)	200	11380	4148.1	2945.1
NLR	1	57	9.0	8.7
ALC (cells/uL)	162.2	9393	1867.0	1213.7
PLR	24	1487	208.6	180.9

Mild cases of Organophosphorus poisoning showed a mean total leukocyte count (TLC) of 11801±4814. An increase in the TLC was noted in moderate cases with a value of 12409.78±4004.01. Severe cases showed further increase in TLC as compared to mild and moderate cases with a value of 19296.41±5952.62. p-value was <0.001 suggesting that TLC is directly proportional to the severity of poisoning. (Table

15) (Figure 10)

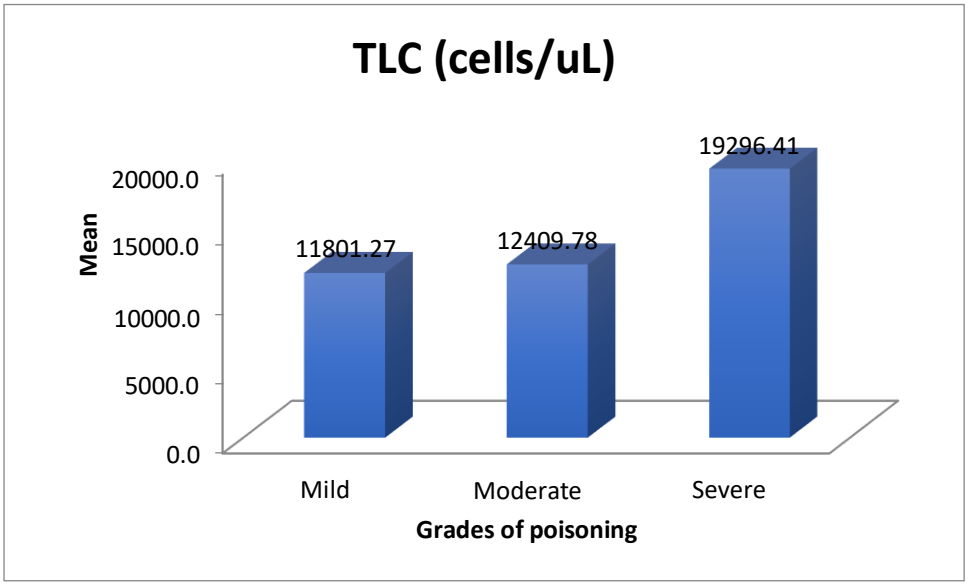
Table 15: Values of Mean TLC in various levels of poisoning

Parameters	POP			p value
	Mild	Moderate	Severe	
TLC (cells/uL)	11801.27± 4814.7	12409.78± 4004.01	19296.41± 5952.62	<0.001 *

Note: * significant at 5% level of significance (p<0.05)

Figure 10:

Comparison of Mean TLC in various levels of poisoning



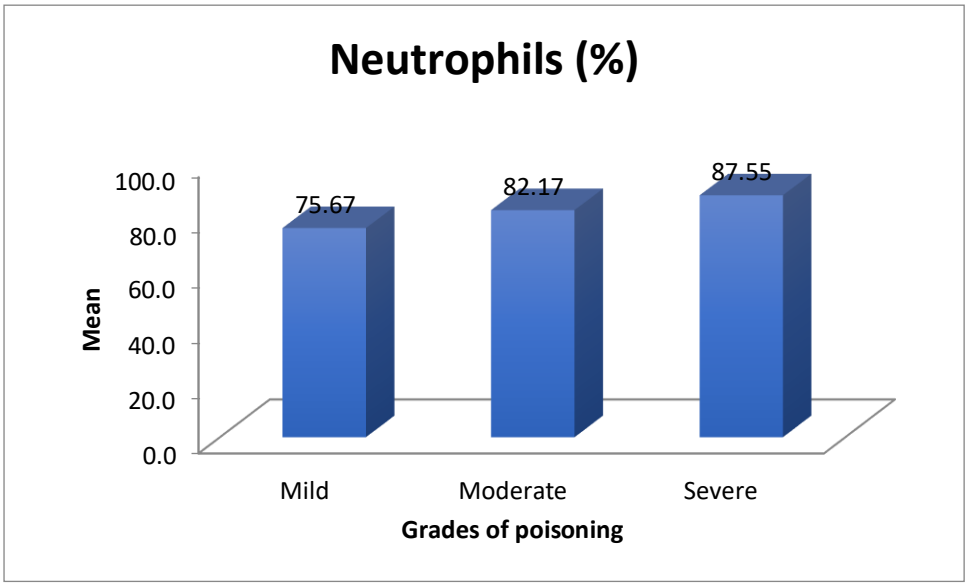
The current study showed an increasing trend in mean Neutrophil count with values of 75.67±12.25, 82.17±6.92 and 87.55±5.66 in mild, moderate and severe cases respectively confirming that neutrophil count is directly proportional to severity of poisoning. (Table 16) (Figure 11)

Table 16: Values of Mean Neutrophil count in various levels of poisoning

Parameters	POP level			p value
	Mild	Moderate	Severe	
Neutrophils (%)	75.67±12.25	82.17±6.92	87.55±5.66	<0.001*

Note: * significant at 5% level of significance (p<0.05)

Figure 11: Comparison of Mean Neutrophil count in various levels of poisoning



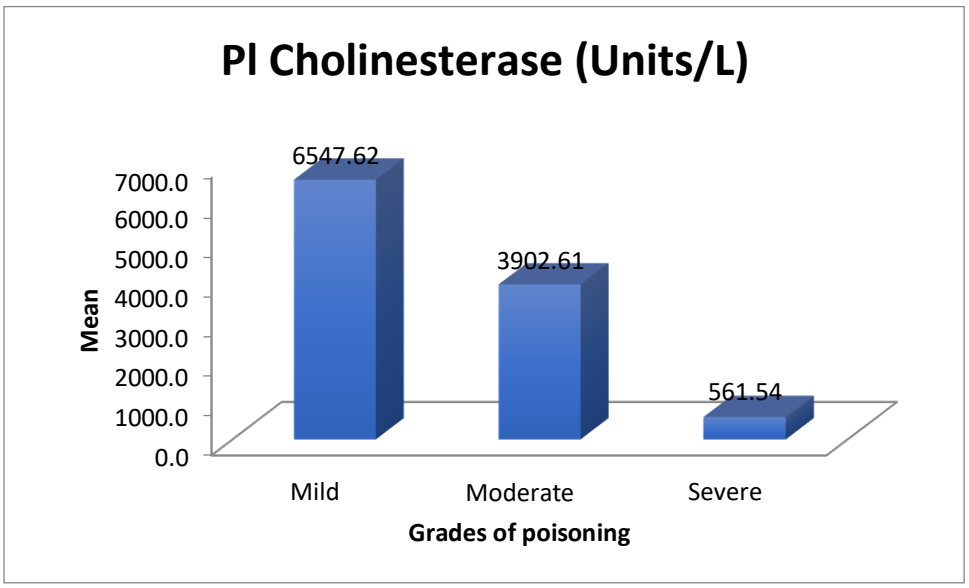
A drop in the mean plasma cholinesterase was noted with values of 6547.62±2121.58 in mild, 3902.61±1646.54 in moderate and 561.54±423.24 in severe cases of Organophosphorus poisoning with a significant p-value of <0.001. This result demonstrates that Plasma cholinesterase is inversely proportional to severity of poisoning in cases of Organophosphorus poisoning. (Table 17) (Figure 12)

Table 17: Values of Mean Plasma Cholinesterase in various levels of poisoning

Parameters	POP			p value
	Mild	Moderate	Severe	
Plasma Cholinesterase (Units/L)	6547.62±2121.58	3902.61±1646.54	561.54±423.24	<0.001*

Note: * significant at 5% level of significance (p<0.05)

Figure 12: Comparison of Mean Plasma Cholinesterase in various levels of poisoning



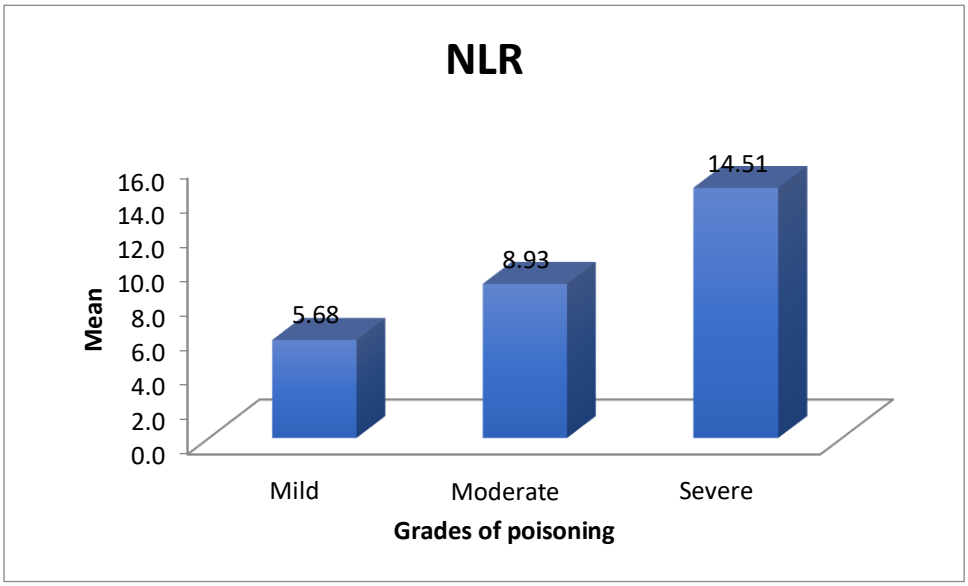
Many studies have proven the authenticity of Neutrophil-lymphocyte ratio in various conditions like sepsis, heart failure etc. In the present study, mean Neutrophil-lymphocyte ratio showed 5.68±4.75 in mild, 8.93±8.72 in moderate and 14.51±10.71 in severe cases with a p-value of <0.001 proving that the values of this parameter increases with increase in the severity of poisoning. (Table 18) (Figure 13)

Table 18: Values of Mean NLR in various levels of poisoning

Parameters	POP			p value
	Mild	Moderate	Severe	
NLR	5.68±4.75	8.93±8.72	14.51±10.71	<0.001*

Note: * significant at 5% level of significance (p<0.05)

Figure 13: Comparison of Mean NLR in various levels of poisoning



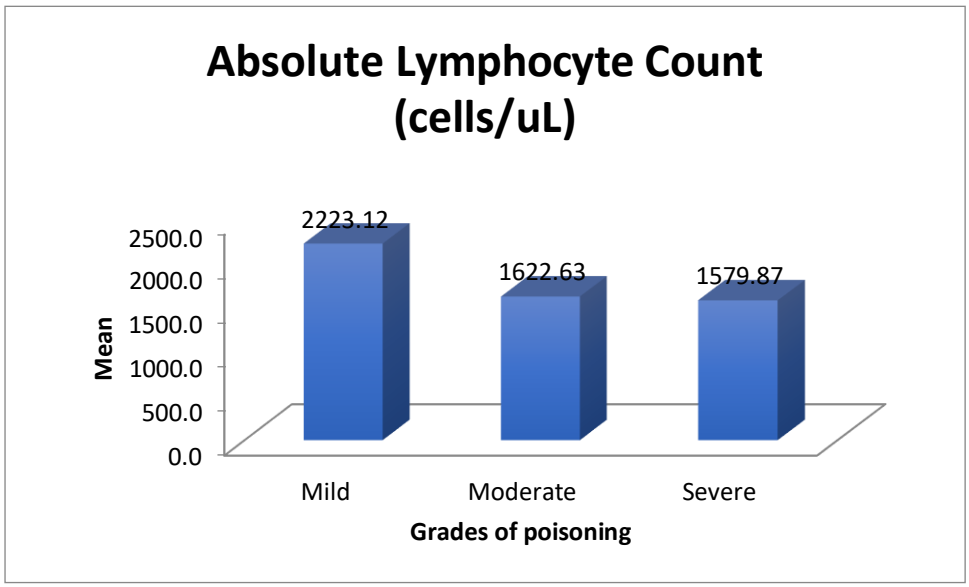
A substantial reduction in the mean absolute lymphocyte count was noted in moderate cases (1622.63±907.02) as compared to mild cases (2223.12±1463.67) of poisoning. Further reduction of lymphocytes was noted in the severe cases (1579.87±928.21) with a p-value of 0.008. This indicates the inversely proportionality of mean ALC to the severity of poisoning. (Table 19) (Figure 14)

Table 19: Values of Mean Absolute Lymphocyte Count in various levels of poisoning

Parameters	POP			p value
	Mild	Moderate	Severe	
Absolute Lymphocyte Count (cells/uL)	2223.12±1463.67	1622.63±907.02	1579.87±928.21	0.008 *

Note: * significant at 5% level of significance ($p<0.05$)

Figure 14: Comparison of Mean Absolute Lymphocyte Count in various levels of poisoning



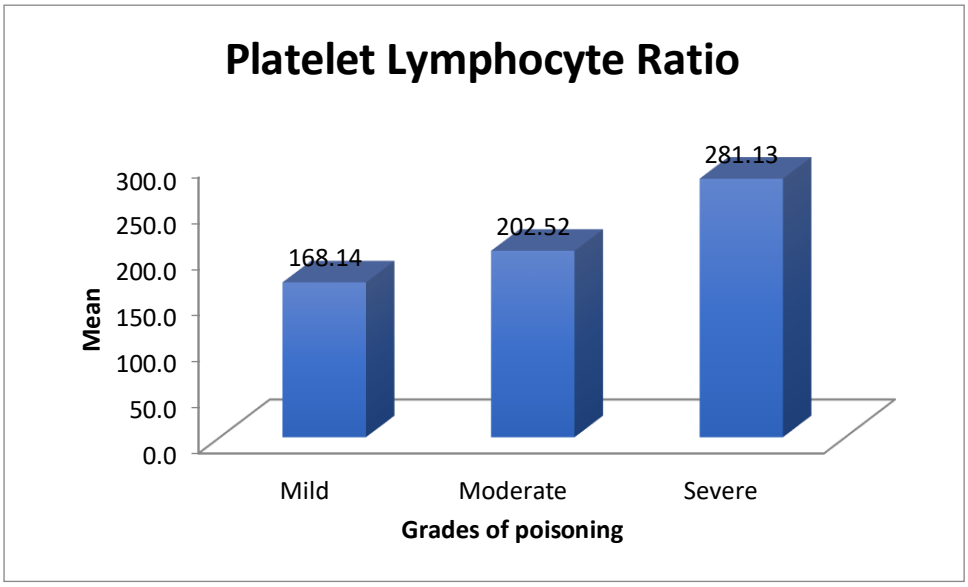
Mean Platelet to lymphocyte ratio (PLR) showed an increasing trend from 168.14±104.18 to 202.52±170.43 and 281.13±257.63 in cases of mild, moderate and severe cases respectively. Hence, PLR is directly proportional to the severity of poisoning. (Table 20) (Figure 15)

Table 20: Values of Mean PLR in various levels of poisoning

Parameters	POP			p value
	Mild	Moderate	Severe	
Platelet lymphocyte ratio (PLR)	168.14±104.18	202.52±170.43	281.13±257.63	0.008*

Note: * significant at 5% level of significance ($p<0.05$)

Figure 15: Comparison of Mean PLR in various levels of poisoning



Receiver Operating Curve (ROC) analysis for 4 variables i.e. Total leukocyte count, Plasma cholinesterase, NLR and PLR was done for predicting mortality. TLC of >15145/uL showed increased chances of mortality with a sensitivity of 71% and a specificity of 69%. Plasma Cholinesterase values <820 Units/L are related to increased mortality with a sensitivity of 86%, a specificity of 84% and a highly significant p-value of <0.001. NLR showed increased chances of mortality with values >8.5 with a sensitivity of 71% and a specificity of 67%. PLR showed increased chances of mortality with values >191 with a sensitivity of 71% and a specificity of 68%. (Table 21, 22)

Table 21: ROC Analysis of parameters in Predicting Mortality

Parameters	Area Under the Curve	Std. Error	p value	95% Confidence Interval	
				Lower	Upper
TLC (cells/uL)	0.73	0.069	0.005*	0.595	0.865
Plasma Cholinesterase (Units/L)	0.93	0.035	<0.001*	0.858	0.996
NLR	0.74	0.063	0.003*	0.62	0.866
PLR	0.75	0.056	0.002*	0.645	0.863

Note: * significant at 5% level of significance (p<0.05)

Table 22: Sensitivity and specificity of lab parameters in predicting mortality

Parameters	Cutoff value	Sensitivity	Specificity
TLC (cells/uL)	15145	71%	69%
Plasma Cholinesterase (Units/L)	820	86%	84%
NLR	8.5	71%	67%
PLR	191	71%	68%

Figure 16: ROC curve of TLC in Predicting Mortality

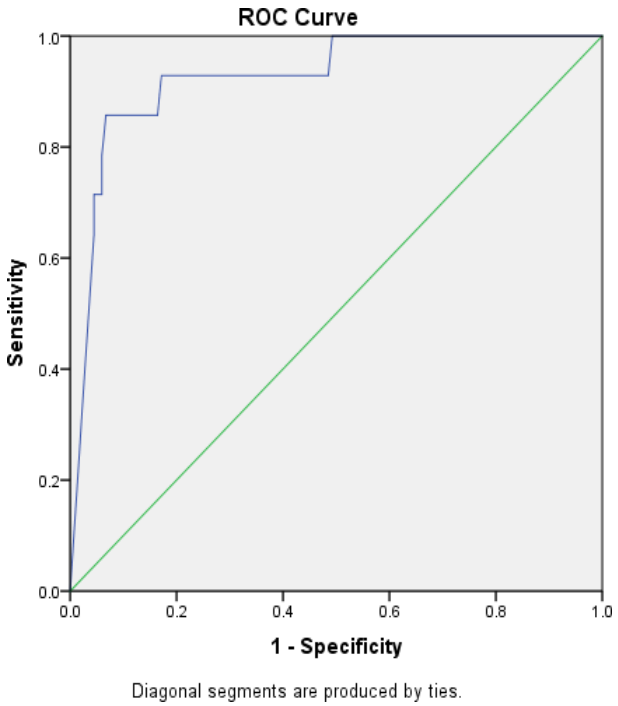


Figure 17: ROC curve of Plasma Cholinesterase in Predicting Mortality

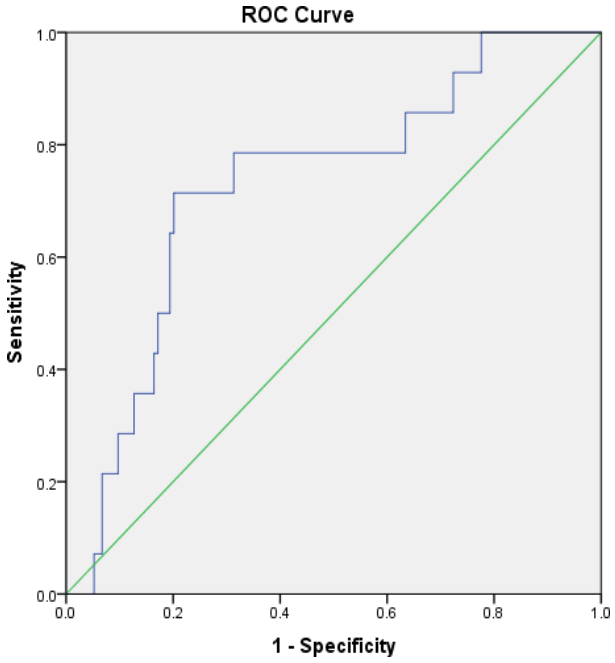


Figure 18: ROC curve of NLR in Predicting Mortality

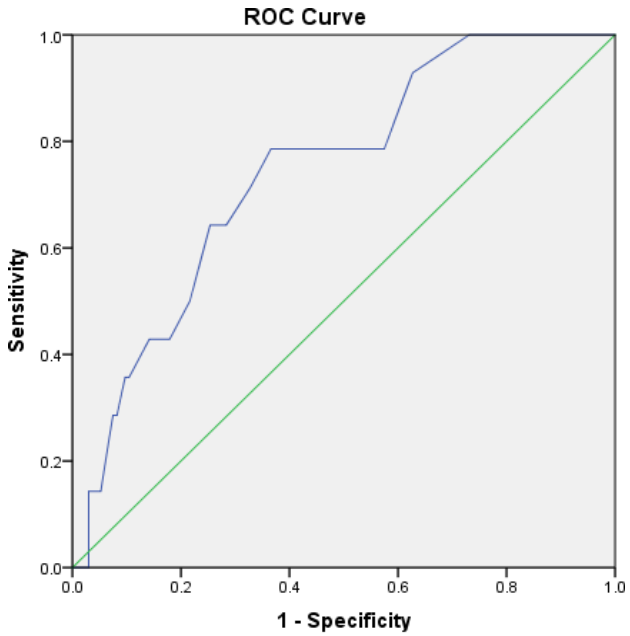
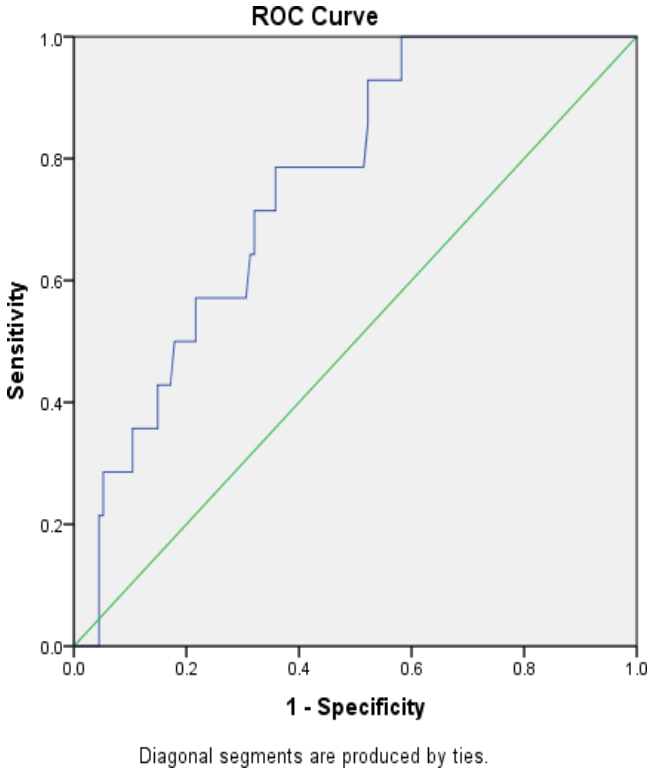


Figure 19: ROC curve of PLR in Predicting Mortality



DISCUSSION

Pesticides are extremely toxic to human beings, and pesticide poisonings are associated with high morbidity and mortality.[1] Self-poisoning with pesticides accounts for 14–20% of global suicides with an estimated 110,000–168,000 deaths each year [35], down from an estimated 371,000 in the late 1990s.[36] The problem is most severe in rural Asian communities, where a wide range of agricultural highly hazardous pesticides (HHPs) are easily available within home and from shops.[37,38,39,40] Acute pesticide poisoning can be accidental, suicidal or homicidal. This study found out that approximately 80% of the poisoning cases in Vijayapura district were suicidal poisoning and 90% of the patients consumed Organophosphorus pesticides followed by Carbamates. In areas like Vijayapura, financial constraints in addition to low rainfall leads to an increased burden of suicidal attempts in the farmer community. Also, over the counter availability of these harmful pesticides makes it much easier to acquire.

"Pesticides are often used impulsively for suicide attempts in times of acute stress, frequently with less than 30 min of planning"[39,41]

The general supportive therapy given to poisoned patients, particularly respiratory and cardiovascular support, are crucial and it is important to decide on admission to the Emergency Department which patient should be followed in the intensive care unit (ICU) and also to estimate which patient can be expected to have a better prognosis during the follow-up period.[1]

After a positive history of pesticide consumption, the recognition of potent prognostic biomarkers is needed during the clinical management of acutely pesticide poisoned- patients to predict the outcome. The clinical significance of basic parameters such as CBC in the diagnosis of poisoning was evaluated by Tang et al.[42]

In general, a pesticide poisoning causes acute oxidative stress which leads to neutrophilic margination, as neutrophils act as the primary reactors in bodily stressful conditions.[1] According to Tang et al[42] the most important indices in predicting mortality in OP poisoning were Neutrophil percentage, followed by Total WBC count, MCHC, and hemoglobin while the most important indices in Paraquat (PQ) poisoning were Platelets, followed by Neutrophil count, Total WBC count and hemoglobin. In the present study mild cases of OP poisoning showed Neutrophil count of 75.67±12.25, moderate cases showed Neutrophil count of 82.17±6.92 and severe cases showed Neutrophil count of 87.55±5.66 suggesting an increase in the Neutrophil count with the grade of poisoning which was in correlation with the study done by Tang et al. (Table 23)

Table 23: Neutrophil count (%) in the present study and other studies

Study	**Mild cases**	**Moderate cases**	**Severe cases**	**p-value**
Tang et al	56±9	82±10	83±13	<0.001
Present study	75.67±12.25	82.17±6.92	87.55±5.66	<0.001

As a primary laboratory abnormality, leukocytosis occurs along with neutrophilia to combat oxidative stress in cases of acute poisoning. In a retrospective study of 209 patients done by Dundar et al[1] it was suggested that more severely poisoned patients had leukocytosis, neutrophilia, monocytosis, and lymphocytopenia within the first 24 h after admission to the ED. Significant leukocytosis in the death group was also noted in studies performed by Kumar S et al[5] and Elhosary NM & Abd-ElBar ES[43]. The present study showed total WBC counts of 11801.27±4814.7 in mild cases of poisoning, 12409.78±4004.01 in moderate cases of poisoning and 19296.41±5952.62 in severe cases of poisoning, hence quadrating with the above

studies. (Table 24)

Table 24: Total Leukocyte count (cells/uL) in the present study and other studies

Study	**Mild cases**	**Moderate cases**	**Severe cases**	**p-value**
Tang et al	5890±1300	14220±6160	18460±8240	<0.001
Kumar et al	7041.35±2405±42	10245.48±4392.69	13440±5130	0.0001
Elhosary NM & Abd-ElBar ES	8210±1050	9550±1420	13320±1050	<0.001
Present study	11801.27±4814.7	12409.78±4004.01	19296.41±5952.62	<0.001

Study done by Elhosary NM and Abd-ElBar ES[43] revealed leukocytosis, lymphopenia, and thrombocytosis in death group. In contradiction, the Absolute Lymphocyte Count (ALC) was increased in the death group of patients with Paraquat poisoning in a study done by Kang C et al.[44] In the present study, the absolute lymphocyte counts of 2223.12±1463.67 in mild cases of poisoning, 1622.63±907.02 in moderate cases of poisoning and 1579.87±928.21 in severe cases of poisoning were noted with a significant p-value of 0.008 suggesting a decrease in ALC with increase in severity of poisoning. This was in agreement with the study done by Elhosary NM and Abd-ElBar ES. (Table 25)

Table 25: Absolute lymphocyte count (cells/uL) in the present study and other studies

Study	**Mild cases**	**Moderate cases**	**Severe cases**	**p-value**
Elhosary NM & Abd-ElBar ES	1670±494.9	1000±70.7	830±56.6	<0.001
Present study	2223.12±1463.67	1622.63±907.02	1579.87±928.21	0.008

Neutrophil to lymphocyte ratio and platelet to lymphocyte ratio have been indicated as fast, feasible and easy to use parameters indicating severity of the oxidative stress in various conditions like sepsis[45], heart failure[46], snake bite[47], Gastrointestinal cancers[48] and poisoning. Several studies undertaken by Elhosary NM & Abd-ElBar ES[43] and Dundar et al[1] showed that Neutrophil to Lymphocyte Ratio and Platelet to Lymphocyte Ratio were statistically elevated in severely poisoned patients. In our study, the relation of neutrophil to lymphocyte ratio with the various levels of poisoning was in agreement with other studies with values of Neutrophil lymphocyte ratio being 5.68±4.75 in mild cases, 8.93±8.72 in moderate cases and 14.51±10.71 in severe cases. (significant p-value of <0.001) (Table 26).

Table 26: Neutrophil to Lymphocyte ratio in the present study and other studies

Study	**Mild cases**	**Moderate cases**	**Severe cases**	**p-value**
Elhosary NM & Abd-ElBar ES	2.09±0.33	3.72±0.59	8.67±2.35	<0.001
Present study	5.68±4.75	8.93±8.72	14.51±10.71	<0.001

The Neutrophil to lymphocyte ratio in the survivors was 8.44±8.48 compared to non survivors who had a Neutrophil to lymphocyte ratio of 14.5±8.9. This was similar to study done by Dundar et al[1] suggesting an increase in the Neutrophil to lymphocyte ratio in non- survivors compared to survivors. (Table 27)

Table 27: Neutrophil to lymphocyte ratio in survivors and non-survivors

Study	**Survivors**	**Non survivors**
Dundar et al	7.3±7.1	11.8±3.6
Present study	8.44±8.48	14.5±8.9

In the present study, the Platelet to lymphocyte ratio in the survivors was 199.55±182.92 compared to non survivors who had a Platelet to lymphocyte ratio of 295.14±137.49. This was similar to study done by Dundar et al[1] suggesting an increase in the Platelet to lymphocyte ratio in non- survivors compared to survivors. (Table 28)

Table 28: Platelet to lymphocyte ratio in survivors and non-survivors

Study	**Survivors**	**Non survivors**
Dundar et al	174.8±118.7	217.2±102.2
Present study	199.55±182.92	295.14±137.49

Platelet lymphocyte ratio was high in severe cases of poisoning as compared to the mild and moderate cases in a study done by Elhosary NM & Abd-ElBar ES. In the present study Platelet lymphocyte ratio was 168.14±104.18 in mild cases of poisoning, 202.52±170.43 in moderate cases of poisoning and 281.13±257.63 in severe cases of poisoning with a p-value of 0.008 which was similar to the study done by Elhosary NM & Abd-ElBar ES. (Table 29)

Table 29: Platelet to lymphocyte ratio in the present study and other studies

Study	**Mild cases**	**Moderate cases**	**Severe cases**
Elhosary NM & Abd-ElBar ES	116.36±25.6	200.63±29	362.51±59.45
Present study	168.14±104.18	202.52±170.43	281.13±257.63

Studies undertaken by Dundar et al[1] and Kumar et al[5] revealed that mean plasma cholinesterase levels was reduced in non-survivors as compared to the survivors. The present study showed mean plasma cholinesterase level of 4520.89±2826.43 in survivors and 580±1098.64 in non-survivors. (Table 30)

Table 30: Plasma cholinesterase (units/L) in survivors and non-survivors

Study	**Survivors**	**Non survivors**	**p-value**
Dundar et al	5449±3919	1667±3025	0.005
Kumar et al	3287.16±2719.30	1456.05±1159.42	0.0001
Present study	4520.89±2826.43	580±1098.64	<0.001

Also, in this study, mean plasma cholinesterase level in mild cases was 6547.62±2121.58, moderate cases was 3902.61±1646.54 and severe cases was 561.54±423.24 with a highly significant p-value of <0.001. This indicates that mean plasma cholinesterase levels were inversely proportional to the severity of poisoning.

In this study we found that there was increase in the various hematological parameters like leukocyte count, neutrophil lymphocyte ratio and platelet lymphocyte ratio with increase in the severity of the pesticide poisoning. The plasma cholinesterase level was noted to decrease with increase in the severity of the pesticide poisoning.

SUMMARY

- A cross sectional study was done on 148 confirmed cases of pesticide poisoning admitted to the casualty for a duration of 1.5 years (1st November 2018 - 30th May 2020).
- Blood samples were collected in EDTA and plain tubes within 24 hours of admission and the values of total leukocyte Count (TLC), neutrophil count, neutrophil-lymphocyte ratio, platelet-lymphocyte ratio and plasma cholinesterase (PChE) were measured and compared.
- The severity of poisoning was assessed according to Peradeniya Organophosphorus (POP) scale.
- As the severity of poisoning increased, there was increase in the TLC with mild cases showing 11801.27±4814.7, moderate cases showing 12409.78±4004.01 and severely poisoned cases showing 19296.41±5952.62 cells/uL.
- Neutrophil count (%) showed an increase from 75.67±12.25 to 82.17±6.92 and 87.55±5.66 in mild, moderate and severe cases of pesticide poisoning respectively.
- Neutrophil to lymphocyte ratio was 5.68±4.75 in mild cases of poisoning, 8.93±8.72 in moderate cases of poisoning and 14.51±10.71 in severe cases of poisoning.
- Platelet to lymphocyte ratio showed an increase with severity of poisoning, from 168.14±104.18 in mild cases to 202.52±170.43 in moderate cases and 202.52±170.43 in severe cases.
- The levels of plasma cholinesterase (Units/L) showed a decrease from 6547.62±2121.58 in mild cases of poisoning to 3902.61±1646.54 in moderate

cases of poisoning and 561.54±423.24 in severe cases of poisoning showing an inversely proportional relationship to the severity of poisoning.

- Hence, total leukocyte count, neutrophil count, neutrophil-lymphocyte ratio and platelet lymphocyte ratio are simple and easy to use parameters that can be used for estimating the severity of pesticide poisoning and assessing its prognosis.

CONCLUSION

- With respect to an increasing death toll due to pesticide poisoning among farmers and lack of specialized instrumentation and technology at the primary care level, few simple and convenient parameters can be used to assess the severity of poisoning, if combined with a history of poison intake.
- Increase in the levels of the total leukocyte counts, neutrophil count, neutrophil lymphocyte ratio and platelet lymphocyte ratio were noted with increasing severity of the pesticide poisoning cases.
- Hence, leukocyte counts, neutrophil count, neutrophil lymphocyte ratio, and platelet lymphocyte ratio within 24 hours of pesticide exposure and prior the administration of any medications are useful, valuable, inexpensive and easily accessible parameters in estimating prognosis and the follow-up of patients with acute pesticide poisoning.

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ANNEXURE-I

B.L.D.E (Deemed to be University)
SHRI.B.M.PATIL MEDICAL COLLEGE HOSPITAL & RESEARCH CENTRE
VIJAYAPUR – 586103

IEC/NO:286/2018
17-11-2018

INSTITUTIONAL ETHICAL COMMITTEE

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Ethical Committee of this college met on 13-11-2018 at 03-15 PM scrutinize the Synopsis of Postgraduate Students of this college from Ethical Clearance point of view. After scrutiny the following original/corrected and revised version synopsis of the Thesis has accorded Ethical Clearance.

Title : Role of leukocyte count, Neutrophil-Lymphocyte ratio & platelet-Lympocyte ratio as a prognostic marker in pesticide poisoning.

Name of P.G. Student : Dr Shubham Chourishi.
Department of Pathology.

Name of Guide/Co-investigator: Dr.B.R.Yelikar, Professor & HOD Department of Pathology.

DR RAGHAVENDRA KULKARNI
CHAIRMAN
Institutional Ethical Committee
BLDEU's Shri B.M. Patil
Medical College,BIJAPUR-586103.

Following documents were placed before E.C. for Scrutinization:

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

BLDE

(DEEMED TO BE UNIVERSITY)

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

The Constituent College

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

BLDE(DU)/REG/PG-Guide/2019-20/994 July 23, 2019

To,
The Professor and HOD
Department of Pathology,
BLDE (DU)'s Shri B. M. Patil Medical College,
Hospital and Research Centre,
Vijayapura

Madam,

Sub: Regarding change of PG Guide.
Ref: Your letter no. Path/2019/637/19 dated 8th July, 2019.

With reference to the subject and letter cited above, on approval of the Hon'ble Vice-Chancellor, the change of PG Guide is permitted in respect of PG Student of your department:

Sl. No.	Name of the Student	Previous Guide	New Guide
1.	Dr. Shashikala H. M.	Dr. B. R. Yelikar	Dr. Surekha B. Hipparagi
2.	Dr. Sahithya H.	Dr. B. R. Yelikar	Dr. R. M. Potekar
3.	Dr. Shubham Chourashi	Dr. Mahesh Karigoudar	Dr. Vijayalaxmi S. Patil

This is for your information and needful.

REGISTRAR

REGISTRAR
BLDE (Deemed to be University)
Vijayapura-586103. Karnataka

Copy to:

- The Dean, Faculty of Medicine and Principal
- The Controller of Examinations
- The Concerned PG Teachers

Noted
Circulate to concerned P.G. students & guides.

Smt. Bangaramma Sajjan Campus, Sholapur Road, Vijayapura – 586103, Karnataka, India.
University: Phone: +918352-262770, Fax: +918352-263303, Website: www.bldedu.ac.in, E-mail: office@bldedu.ac.in
College: Phone: +918352-262770, Fax: +918352-263019, Website: www.bldedu.ac.in, E-mail: bmpmc.principal@bldedu.ac.in

ANNEXURE-II

B.L.D.E (DEEMED TO BE) UNIVERSITY, SHRI B.M.PATIL MEDICAL COLLEGE HOSPITAL AND RESEARCH CENTER, VIJAYAPURAA-586103

INFORMED CONSENT FOR PARTICIPATION IN DISSERTATION/RESEARCH

I, the undersigned,_____, S/O D/O W/O_____, aged ____years, ordinarily resident of_____ do hereby state/declare that Dr _____ of

_____Hospital has examined me thoroughly on _____at_____(place) and it has been explained to me in my own language that I am suffering from_____disease (condition) and this disease/condition mimic following diseases. Further Doctor informed me that he/she is conducting dissertation/research titled_____under the guidance of

Dr_____ requesting my participation in the study. Apart from routine treatment procedure, the pre-operative, operative, post-operative and follow-up observations will be utilized for the study as reference data.

Doctor has also informed me that during conduct of this procedure adverse results may be encountered. Among the above complications most of them are treatable but are not anticipated hence there is chance of aggravation of my condition and in rare circumstances it may prove fatal in spite of anticipated diagnosis and best treatment made available. Further Doctor has informed me that my participation in this study will help in evaluation of the results of the study which is useful reference to treatment of other similar cases in near future, and also I may be benefited in getting relieved of suffering or cure of the disease I am suffering.

The Doctor has also informed me that information given by me, observations made/ photographs/ video graphs taken upon me by the investigator will be kept secret and not assessed by the person other than me or my legal hirer except for academic purposes.

The Doctor did inform me that though my participation is purely voluntary, based on information given by me, I can ask any clarification during the course of treatment / study related to diagnosis, procedure of treatment, result of treatment or prognosis. At the same time I have been informed that I can withdraw from my participation in this study at any time if I want or the investigator can terminate me from the study at any time from the study but not the procedure of treatment and follow-up unless I request to be discharged.

After understanding the nature of dissertation or research, diagnosis made, mode of treatment, I the undersigned Shri/Smt_____under my full conscious state of mind agree to participate in the said research/dissertation.

Signature of patient:

Signature of doctor:

Witness: 1.

2.

Date:

Place

ANNEXURE-III

PROFORMA

NAME	:	OP/IP No.	:
AGE	:		
SEX	:	D.O.A	:
RELIGION	:	D.O.D	:
OCCUPATION	:		
RESIDENCE	:		
Presenting Complaints	:		
Past history	:		
Personal history	:		
Family history	:		
Treatment history	:		

General physical examination**:**

Pallor	present/absent
Icterus	present/absent
Clubbing	present/absent
Lymphadenopathy	present/absent
Edema	present/absent
Built	poor/average/well

VITALS: PR: RR:

BP: TEMPERATURE:

WEIGHT:

SYSTEMIC EXAMINATION:

Cardiovascular system:
Respiratory system:
Per Abdomen:
Central nervous system:
Clinical Diagnosis:

INVESTIGATIONS:

Hematological Investigations:

Parameters:	Normal Range:	Patient Values:
Hemoglobin (gm/dl)	Males- 13-16 Females- 12-14	
Red cell distribution width-coefficient of variation (RDW-CV) (%)	39-46	
Total Leukocyte Count (/uL)	4000-11000	
Platelet Count ($x10^5$/uL)	1.5-5	
Neutrophils (%)	40-80	
Lymphocytes (%)	20-40	
Eosinophils (%)	1-6	
Monocytes (%)	2-10	
Basophils (%)	<1-2	
Neutrophil-Lymphocyte ratio	2:1-2.67:1	
Platelet-Lymphocyte ratio	150-166.67	

Biochemical investigation:

Plasma Cholinesterase (U/L)	5000–12,000	

Key to Master Chart

1. Sr. No.	Serial Number
2. IP	In Patient number
3. TLC	Total Leukocyte Count
4. Hb	Hemoglobin
5. PCV	Packed cell volume
6. MCV	Mean corpuscular volume
7. MCH	Mean corpuscular hemoglobin
8. MCHC	Mean corpuscular hemoglobin concentration
9. RDW	Red cell distribution width
10. PChe	Plasma Cholinesterase
11. NLR	Neutrophil lymphocyte ratio
12. ALC	Absolute lymphocyte count
13. PLR	Platelet lymphocyte ratio
14. POP	Peradeniya Organophosphorus Poisoning scale
15. S	Survivors
16. NS	Non survivors
17. C	Carbamate
18. OP	Organophosphorus
19. S	Suicidal
20. H	Homicidal
21. A	Accidental

MASTER CHART

Sr. No.	IP	Age/Sex	TLC (cells/uL)	Neutrophils (%)	Lymphocytes (%)	Eosinophils (%)	Monocytes (%)	Basophils (%)	Hb (gm/dl)	PCV (%)	MCV (fL)	MCH (pg)	MCHC (%)	Platelet (cells/uL)	RDW (%)	PChe (Units/L)	NLR	ALC (cells/uL)	PLR	POP	Survivors/ Non Survivors	Type of poison	S/H/A
1	41685/18	30/F	11800	84.7	11.4	1.3	2.5	0.1	12.8	38.9	95.8	31.5	32.9	326000	12	8890	7	1345	242	1	S	OP	S
2	42163/18	18/F	10520	77.9	18.6	0.2	3.2	0.1	8.1	26.6	68.6	20.9	30.5	316000	20.3	3760	4	1956	161	2	S	OP	S
3	42161/18	25/M	7390	59.2	28.1	9.2	3.1	0.4	15.1	44.4	95.3	32.4	34	243000	12.8	9870	2	2076	117	1	S	OP	S
4	42418/18	17/F	22910	93.4	4.1	0	2.4	0.1	13.7	42	88.8	29	32.6	363000	13.3	4670	22	9393	38	1	S	OP	S
5	42429/18	14/M	8080	71	22.5	0.1	6.3	0.1	11.4	35.3	77.8	25.1	32.3	269000	14.4	6030	3	1818	147	1	S	OP	H
6	41640/18	20/F	1850	78.4	17.5	0.6	3.4	0.1	15.8	47.3	86	28.7	33.4	366000	13	7950	4	3253	112	1	S	OP	S
7	41054/18	27/F	20670	84.4	13.6	0.5	1	0.1	13.8	41.6	90.6	30.1	33.2	307000	12	6860	6	2811	109	1	S	OP	S
8	40894/18	32/M	8970	52.1	36.2	5.7	5.6	0.4	15.2	49.3	70	21.6	30.8	244000	17.8	7970	1	3247	75	1	S	OP	S
9	40905/18	40/M	14090	85	11.3	0.1	3.5	0.1	14	41.8	77.7	26	33.5	200000	12.9	4240	7	1592	125	1	S	OP	A
10	42564/18	27/F	13190	83.4	11.7	0	4.8	0.1	9.9	34	71.7	20.9	29.1	355000	20.7	8460	7	1543	230	1	S	OP	S
11	42582/18	28/M	8910	85.4	12.1	0.3	2.1	0.1	15.1	43.7	93.8	32.4	34.6	234000	13.8	7790	7	1078	217	1	S	OP	A
12	42687/18	40/F	11490	73.7	23.2	0.3	2.7	0.1	12.9	37.2	78.3	27.2	34.7	379000	13.9	4320	3	2666	142	1	S	C	S
13	42698/18	25/F	14740	69.2	26.5	0.9	3.3	0.1	13.1	39.3	85.1	28.4	33.3	311000	12.5	4110	2	3906	79	1	S	C	S
14	42731/18	35/F	19740	94.1	4.9	0	0.9	0.1	13	39.6	88.8	29.1	32.8	326000	13.2	8400	19	967	337	2	S	OP	S
15	43095/18	35/F	20600	90.4	8.9	0	0.7	0	15.7	49.5	103.1	32.7	31.7	462000	13.9	10220	10	1833	252	1	S	OP	A
16	42974/18	26/F	11210	90.1	7.5	0	2.3	0.1	11.5	35.8	74.3	23.9	32.1	416000	16	200	12	840	495	3	NS	OP	S
17	42973/18	24/F	9490	81.2	14.9	0.1	3.8	0	11	35.4	69.1	21.5	31.1	500000	18.4	200	5	1414	353	3	NS	OP	S
18	43029/18	15/F	9180	70	24.7	0.1	5.2	0	9.9	32.2	80.7	24.8	30.7	412000	16.7	5180	2	2267	181	1	S	C	H
19	43181/18	18/F	21150	86.1	9.8	0	4	0.1	12.9	37.2	102.5	35.5	34.7	398000	12.9	200	8	2072	192	3	NS	OP	S
20	43182/18	20/M	39030	89.2	9.2	0.1	1.4	0.1	17.7	54.7	93.8	30.4	32.4	435000	13.7	200	9	3590	121	3	S	OP	S
21	43343/18	37/M	7970	64.1	27.1	5.1	3.6	0.1	13	40.2	95.3	30.8	32.3	292000	14	8930	2	2159	135	2	S	C	S
22	43436/18	17/M	11850	68.5	25.2	2.5	3.6	0.2	14.9	43.5	81.6	28	34.3	310000	13	1020	2	2986	103	3	S	OP	H
23	43438/18	48/M	26440	78	2	1	0	0	16.2	48.9	100.8	33.4	33.1	356000	14.1	8590	39	5288	67	2	S	OP	S
24	43489/18	19/F	23550	69.3	26.8	0.5	3.4	0	9.8	31.7	78.3	24.2	30.9	637000	14.3	200	2	6311	100	1	S	OP	A
25	43619/18	32/M	10230	84.8	11.4	0.1	3.5	0.2	13.2	37.8	90	31.4	34.9	314000	12.8	8800	7	1166	269	1	S	C	S
26	43663/18	45/M	7810	70.3	25.4	1	3.3	0	16.3	47.1	79.7	27.6	34.6	192000	12.9	11380	2	1983	96	1	S	OP	S
27	43847/18	22/M	9000	73.9	18.3	3.6	4.1	0.1	14.9	43.8	90.7	30.8	34	244000	12.5	4840	4	1647	148	1	S	OP	S
28	43858/18	25/F	13450	90.5	7	0.1	2.3	0.1	12	38.7	75	23.3	31	300000	14.2	8610	12	941	318	1	S	OP	S
29	43976/18	52/M	7330	48.5	31.7	15	4.5	0.3	14.4	42.4	84.5	28.7	34	206000	14	6970	1	2323	88	1	S	OP	A
30	43981/18	23/F	12210	71.5	23.1	0.5	4.8	0.1	9.6	33.4	69.6	20	28.7	530000	15.6	4420	3	2820	187	1	S	OP	S
31	44044/18	24/F	9720	63.7	29.4	3.8	2.9	0.2	11.2	35.4	91	28.8	31.6	311000	12.8	6010	2	2666	116	1	S	OP	S
32	44065/18	20/M	15700	87.3	9	0.3	3.2	0.2	17.3	48.8	92.4	32.8	35.5	238000	14.5	3420	9	1413	168	1	S	OP	S
33	149/19	28/M	6160	55.7	35.1	2.3	6.7	0.2	15.5	42.5	88.2	32.2	36.5	220000	12.6	9600	1	2162	101	1	S	OP	S
34	403/19	21/F	15820	85	10.8	0.4	3.7	0.1	12.2	39.9	77.3	23.6	30.6	323000	26.4	9540	7	1708	189	1	S	OP	S
35	405/19	20/M	11030	88.2	8.3	1.8	1.5	0.2	15.2	45.6	98.3	32.8	33.3	296000	14	9320	10	915	323	1	S	OP	A
36	16543/19	26/M	17270	90.6	8	0.1	1.2	0.1	15.6	46	84.9	28.8	33.9	202000	12.2	220	11	1381	146	3	NS	OP	S
37	16311/19	28/M	26170	82.9	13.3	1.3	2.3	0.2	16.9	51.8	92.7	30.2	32.6	325000	12.1	260	6	3480	93	3	S	OP	S
38	15931/19	18/F	13910	83.9	13	0	3	0.1	11.4	34.2	84.2	28.1	33.3	302000	14	4780	6	1808	167	2	S	OP	H

39	15711/19	30/F	14670	88	8	1.2	2.7	0.1	15.2	42.3	93.4	33.6	35.9	183000	14.6	1630	11	1173	156	2	S	OP	A
40	15633/19	26/F	3120	70.9	23.7	0	5.4	0	10.9	34.7	76.8	24.1	31.4	205000	16.1	6640	2	739	277	1	S	C	S
41	15479/19	30/M	12040	85.4	11.2	0.7	2.5	0.2	16.6	47.7	108.4	37.7	34.8	267000	14.5	7790	7	1348	198	2	S	OP	S
42	15052/19	16/F	14070	72.2	24	0.1	3.6	0.1	12.5	37	100.5	34	33.8	354000	14.6	4860	3	3376	104	1	S	OP	H
43	14938/19	16/M	16910	97.1	1.7	0	1.1	0.1	11.8	37.1	82.8	26.3	31.8	427000	18.8	200	57	287	1487	3	S	OP	S
44	14918/19	23/M	11910	50	45.7	0.9	2.9	0.5	13.9	41	95.3	32.3	33.9	222000	12.7	5330	1	5442	40	1	S	OP	H
45	14870/19	30/F	20980	91.7	5.8	0.1	2.2	0.2	12.3	37.9	90.7	29.4	32.5	346000	13.3	200	15	1216	284	3	S	OP	S
46	14761/19	32/M	9500	82.8	15.1	0.3	1.7	0.1	15.6	43.8	88.8	31.6	35.6	229000	12.9	3020	5	1434	159	2	S	OP	A
47	14513/19	28/F	13650	89.5	7.1	0.1	3.2	0.1	11	36.1	84.1	25.6	30.5	280000	16.2	5510	12	969	288	1	S	OP	S
48	14106/19	25/F	8540	70.9	21.2	2.9	4.8	0.2	12.8	38.3	88.7	29.6	33.4	292000	12.9	7710	3	1810	161	1	S	OP	S
49	14104/19	25/M	6520	65.6	28.1	1.7	4.4	0.2	13.2	40	85.1	28.1	33	262000	17.6	3870	2	1832	143	2	S	C	S
50	13712/19	28/M	8230	66.3	29.5	0.4	3.6	0.2	15.5	46.6	95.1	31.6	33.3	362000	13.1	5600	2	2427	149	1	S	OP	A
51	13471/19	25/F	17710	84.7	8.5	0	6.7	0.1	12.4	39.2	99	31.3	31.6	392000	18.6	200	9	1505	260	3	NS	OP	S
52	13293/19	55/M	13690	81.7	12.3	1.5	4.4	0.1	14.9	46.7	91.9	29.3	31.9	191000	13.3	1130	6	1683	113	3	S	OP	S
53	13117/19	38/M	9240	81.1	14.9	0.1	3.8	0.1	12	35.9	97.8	32.7	33.4	99000	13.2	3030	5	1376	71	2	S	OP	S
54	12255/19	30/M	11380	89.9	6.4	0.2	3.3	0.2	16.9	52	90.6	29.4	32.5	302000	13.2	6840	14	728	414	1	S	OP	S
55	11591/19	35/F	11560	91.5	6.7	0.1	1.6	0.1	13.2	38.9	91.1	30.9	33.9	262000	12.9	340	13	774	338	3	S	OP	S
56	11535/19	34/M	5270	52.1	41.9	0.9	4.7	0.4	13.8	40.1	88.7	30.5	34.4	253000	12.8	9050	1	2208	114	1	S	OP	S
57	11435/19	19/F	15780	90.7	6.1	0.1	2.9	0.2	8.4	29.6	81.1	23	28.4	339000	17.2	6150	14	962	352	1	S	C	H
58	11263/19	23/F	9660	80.2	16.3	0.4	3	0.1	12.2	37.8	93.1	30	32.3	309000	12.5	8450	4	1574	196	1	S	OP	S
59	10763/19	12/M	10360	48	47.2	1.2	3.4	0.2	11.5	34	85	28.8	33.8	274000	12.9	8940	1	4889	56	1	S	OP	H
60	10257/19	25/F	3900	74.1	20.8	1.5	3.1	0.5	7.8	24.3	97.2	31.2	32.1	117000	14.7	3800	3	811	144	2	S	OP	S
61	10129/19	28/F	15660	91.6	6.6	0.5	1.2	0.1	13.1	38.8	89	30	33.8	228000	13.1	6640	13	1033	220	1	S	OP	A
62	9431/19	25/M	15090	65.3	30.2	1.1	2.9	0.5	15.2	46.8	98.3	31.9	32.5	273000	13.2	8760	2	4557	59	1	S	OP	S
63	9168/19	19/F	13550	90.9	5.8	0	3.2	0.1	13.2	37.8	108.9	38	34.9	282000	13.7	1320	15	785	359	2	S	OP	S
64	9086/19	45/F	17080	95.1	4.2	0	0.6	0.1	12.9	39	90.7	30	33.1	278000	12.6	800	22	717	387	1	S	OP	H
65	9167/19	52/M	5770	48.8	42.3	3.6	5	0.3	13.6	42	93.5	30.3	32.4	208000	12	5870	1	2440	85	1	S	C	S
66	8670/19	23/F	12050	94.6	3.6	0.1	1.6	0.1	10.5	32.4	92.4	26.7	32.4	281000	13.1	840	26	433	648	3	S	OP	S
67	8984/19	38/M	8120	68.3	20.7	5.2	5.7	0.1	7	21.4	97.3	31.8	32.7	113000	15.8	5420	3	1680	67	1	S	OP	H
68	8314/19	30/F	29730	88.7	8	0.3	2.8	0.2	13.7	42.2	81.2	26.3	32.5	289000	14.1	200	11	2378	121	3	S	C	S
69	7501/19	30/M	10720	88.7	9	0	2.2	0.01	11.1	38.2	79.1	23	29.4	361000	17.5	6800	9	2378	151	1	S	OP	S
70	17108/19	21/F	23350	85.6	7.7	0	6.7	0	8.4	24.6	85.4	29.2	34.1	264000	13.8	8720	11	1797.95	146	1	S	OP	S
71	17675/19	45/M	12600	85.5	9.5	0.2	3	0.2	11.1	33.3	85.6	28.5	33.3	164000	13.7	2480	9	1197	137	2	S	OP	S
72	17654/19	68/M	21830	72.8	14	0.1	5.2	0.1	9.3	25.5	84.5	30.8	36.5	90000	17.3	4800	5	3056.2	29	1	S	OP	H
73	17663/19	38/F	10040	78	16.1	0.5	3.5	0.7	11.7	34.6	93.2	31.5	33.8	218000	15.6	4320	4	1616.44	134	2	NS	OP	S
74	17673/19	42/M	11190	83.2	10.5	0.2	4.7	0.6	17.4	52.3	87.8	29.3	33.3	216000	14.6	3900	7	1174.95	183	2	S	OP	S
75	17678/19	58/M	19780	78.3	8.7	2.9	2.9	0.2	11.3	32.7	94.2	32.4	34.4	194000	15.4	4800	9	1720.86	112	1	S	OP	H
76	17560/19	36/F	29730	90	7	0	3	0	6	19.1	65.7	20.7	31.5	66000	19.3	500	12	2081.1	31	3	S	OP	S
77	17492/19	52/M	12550	90.5	3.7	0.1	4.7	0	12.8	38.9	79.8	26.3	33	170000	14.8	800	24	464.35	366	3	S	OP	S
78	17324/19	48/F	18470	92	3.5	0.4	1.8	0.7	7.9	23.5	86.9	29.4	33.9	141000	16.9	420	26	646.45	218	3	S	OP	S
79	17515/19	50/F	15200	85	13	1	1	0	9.6	29.7	86.1	27.8	32.3	237000	15	2440	6	1976	119	2	S	C	S
80	17377/19	46/F	12320	88	5	1	0	0	10.4	30.1	97.2	33.6	34.6	285000	18.5	3680	17	616	462	2	S	OP	H
81	17628/19	44/M	13060	68.7	20.2	5.7	3.5	0.7	12.1	37.9	66.5	21.2	31.8	397000	16.8	4460	3	2638.12	150	2	S	OP	S
82	17509/19	30/F	12370	69.3	23.3	1.1	4.8	0.5	12.4	33.4	84.5	31.3	37	71000	15.5	4580	2	2882.21	24	2	S	OP	S
83	17653/19	18/M	22150	79.8	14	0.3	3.5	0.3	9.7	33.1	64.7	19	29.4	523000	17.2	2980	5	3101	168	2	S	OP	S
84	17040/19	46/M	14800	82	15	2	1	0	8.4	25.6	105	34.6	32.8	437000	15.8	1020	5	2220	196	3	NS	OP	S
85	17530/19	22/M	11880	72.8	21.2	2.4	1.9	0	8.8	26.5	89.7	29.9	33.4	266000	14	5980	3	2518.56	105	1	S	OP	S
86	17504/19	20/F	12520	81.3	12.3	1.6	3.2	0.1	12.5	37.6	84	27.9	33.3	205000	15.9	3760	6	1539.96	133	2	S	OP	H

87	17175/19	52/M	17220	93.3	2.7	0.2	2	0	15	43.2	90.3	31.3	34.6	367000	14.8	400	34	464.94	789	3	S	OP	S
88	17418/19	70/M	12550	88	10	2	0	0	8.5	25.1	80.4	27.2	33.9	412000	12.7	2680	8	1255	328	2	S	OP	S
89	17639/19	26/M	16060	76.1	16.2	2.7	3.6	0.3	9.5	30.8	67.3	20.7	30.7	316000	16.7	4680	4	2601.72	121	1	S	C	H
90	17640/19	19/F	14180	81.4	9.4	2.2	3.8	0.5	8.7	26.7	78.4	25.6	32.7	226000	16.5	3620	8	1332.92	169	2	S	OP	H
91	17635/19	28/F	17780	86.3	7.6	0.2	4.2	0.2	6.9	23.6	57.4	16.8	29.3	337000	18.7	2120	11	1351.28	249	2	S	OP	S
92	17634/19	28/F	16230	81.1	14.4	0.6	1.6	0.4	8.6	26.9	86.8	27.7	32	244000	25.1	2340	5	2337.12	104	2	S	OP	S
93	17633/19	25/F	17850	88.3	7.1	0.2	2.7	0.5	11.6	36.3	96.3	30.7	31.9	270000	15.1	800	12	1267.35	213	3	S	OP	S
94	17644/19	28/F	17160	81.4	13	0.4	3.8	0.3	9	29	73.4	22.7	31	295000	19.3	1320	6	2230.8	132	3	S	OP	S
95	17643/19	29/F	14160	77.7	17.3	0.7	2.6	0.6	9.4	29	82.3	26.7	32.4	213000	16.8	5100	4	2449.68	86	1	S	C	S
96	17630/19	21/F	23060	91.4	4.9	0.3	2	0.2	11	35.4	78	24.2	31.1	363000	21.1	200	18	1129.94	321	3	NS	OP	H
97	17515/19	22/F	15200	85	13	1	1	0	9.6	29.7	86.1	27.8	32.3	237000	15	1220	6	1976	119	3	S	OP	S
98	17622/19	62/M	20520	84.1	7	0.4	5.8	0.1	10.1	30.9	82.7	27	32.7	169000	15.1	800	12	1436.4	117	3	S	OP	S
99	16555/19	74/M	4990	90	6	2	2	0	6.2	18.9	63.6	20.9	32.8	100000	38.5	6860	15	299.4	334	1	S	OP	S
100	18198/19	63/M	18510	89.6	8.1	0	2.1	0.2	15.4	44.4	84.9	29.4	34.7	218000	12.9	400	11	1499.31	145	3	NS	OP	S
101	18095/19	83/F	14150	84.6	10.6	0.1	4.3	0.4	9.8	28.6	85.1	29.2	34.3	255000	14.2	1860	7	1499.9	170	3	S	OP	S
102	18455/19	23/F	17170	78	17	2	3	0	12.6	38.1	84.1	27.8	33.1	179000	14.2	3620	4	2918.9	61	2	S	OP	S
103	18313/19	23/F	23100	94.8	4.2	0	1	0	10.5	32.3	78.2	25.4	32.5	460000	19.7	200	22	970.2	474	3	NS	OP	H
104	18427/19	52/F	6460	64.7	27.2	2.2	5.3	0.6	10.9	33.8	88.7	28.6	32.2	357000	14.6	7680	2	1757.12	203	1	S	OP	S
105	18379/19	45/M	11340	91.4	4.1	0.5	3.6	0.4	9.6	28	88.1	30.2	34.3	328000	13.2	3680	22	464.94	705	2	S	OP	S
106	18483/19	30/M	12590	66	25	2	7	0	14.4	45.9	72.9	22.8	31.3	323000	15.1	7980	2	3147.5	102	1	S	C	S
107	17982/19	48/M	26140	92	5	2	1	0	13.6	39.8	88.3	30.1	34.1	247000	16.2	200	18	1307	188	3	S	OP	S
108	18441/19	25/F	13110	76	18	6	0	0	7.7	24.6	68.2	21.3	31.2	267000	18.4	2080	4	2359.8	113	2	S	OP	S
109	18431/19	60/M	9920	77	16	1	6	0	15.5	44.6	93	32.2	34.6	165000	15.7	8980	4	1587.2	103	1	S	OP	S
110	18426/19	26/F	12280	85	12	0	3	0	12.5	36.9	91	30.9	33.9	229000	13.8	3720	7	1473.6	155	2	S	OP	S
111	17760/19	25/F	25390	94	3	3	0	0	14.7	44.1	88.6	29.5	33.3	380000	19.4	200	31	761.7	498	3	NS	OP	S
112	17746/19	53/F	8310	90	6	1	3	0	9.3	31.1	65.6	19.6	29.9	121000	17.6	4620	15	498.6	242	2	S	OP	S
113	18435/19	65/M	10660	89.9	6.8	0	3.1	0.2	13.1	37.8	81.5	28.2	34.7	300000	12.6	4760	13	724.88	413	2	S	OP	S
114	18439/19	23/F	9620	91	6	1	2	0	13	38.7	89.8	30.1	33.5	257000	17.9	3800	15	577.2	445	2	S	OP	S
115	18454/19	26/F	12740	78.2	17.7	0.5	3.4	0.2	10	30.7	72.4	23.6	32.6	230000	13.7	3680	4	2254.98	101	2	S	OP	S
116	18453/19	56/M	16000	86.4	9.2	0.1	4.1	0.2	14.6	43.6	70.2	23.5	33.5	427000	13.9	780	9	1472	290	3	S	OP	S
117	17171/19	50/F	9910	84	14	1	1	0	13.6	41.6	79.4	26	32.7	192000	16.1	3780	6	1387.4	138	2	S	OP	S
118	18446/19	24/F	10850	83	13	4	0	0	12.6	39.1	79.7	25.7	32.2	210000	15.9	3800	6	1410.5	148	2	S	OP	S
119	18128/19	28/F	26570	84	10	2	4	0	11.1	34.6	81.1	26.1	32.1	130000	23.5	620	8	2657	48	3	S	OP	S
120	18385/19	18/F	17280	84	10	2	4	0	9.4	27.1	91.3	31.7	34.8	167000	16.8	2290	8	1728	96	2	S	OP	H
121	18451/19	24/F	9660	74	22	2	2	0	14.5	44	85.3	28.2	33	307000	17.6	4820	3	2125.2	144	2	S	OP	S
122	18465/19	65/F	6930	85	12	1	2	0	12.4	36.7	87.7	29.5	33.7	123000	14.5	5320	7	831.6	147	1	S	OP	S
123	18470/19	55/M	12740	80	12	2	6	0	10.9	34.8	83.7	26.3	31.4	203000	14.7	5280	6	1528.8	132	1	S	C	S
124	18469/19	38/M	20470	90	6	1	3	0	13.8	40.8	96.4	32.7	33.9	354000	16.3	200	15	1228.2	288	3	NS	OP	S
125	18398/19	35/F	14100	77	20	1	2	0	7.6	23	80.2	26.6	33.1	189000	17.6	3280	3	2820	67	2	S	OP	S
126	18463/19	36/M	11220	82	14	1	3	0	12.8	38.2	96.9	32.5	33.5	174000	16.6	3640	5	1570.8	110	2	S	OP	S
127	18464/19	71/M	10200	85	10	2	3	0	11.6	34.7	84.7	28.2	33.3	316000	15	4420	8	1020	309	2	S	OP	S
128	18407/19	31/F	21640	75	20	2	3	0	10.9	31.7	96.9	33.3	34.3	261000	14.3	1440	3	4328	60	3	S	OP	S
129	18467/19	27/F	20420	87	8	2	3	0	9.1	28.9	72.5	22.9	31.6	347000	18.3	640	10	1633.6	212	3	S	OP	S
130	18430/19	65/F	10750	82	13	2	3	0	14.5	43.8	83.2	27.5	33	215000	14.5	3680	6	1397.5	153	2	S	OP	S
131	17800/19	68/M	8110	95	2	3	0	0	14.3	42.4	84.1	28.3	33.6	155000	14.6	4110	47	162.2	955	2	S	OP	S
132	18449/19	25/M	11790	87	11	2	0	0	14.2	42.2	97.1	32.8	33.8	735000	15.7	5850	7	1296.9	566	1	S	OP	S
133	18442/19	52/M	13150	87.1	8.7	0.3	3.7	0.2	13.1	37.1	84.9	30	35.3	100000	12.9	2310	10	1144.05	87	2	S	OP	S
134	17706/19	64/M	20350	91	5	2	2	0	14.8	44.3	89.5	29.9	33.5	269000	13.8	800	18	1017.5	264	3	S	OP	S

135	18437/19	75/M	17350	88	4	2	6	0	12.9	39.3	78.3	25.7	32.8	127000	13.6	360	22	694	182	3	NS	OP	S
136	19057/19	18/F	13400	76.6	20.3	1.3	0.4	0.7	14.2	42.6	90.5	30	33.2	379000	14.7	3280	3	2720.2	139	2	S	OP	H
137	19018/19	22/F	18560	81.2	13.4	4.1	0.2	0.2	10.6	32.9	76	24.6	32.4	391000	15.2	680	6	2487.04	157	3	S	OP	S
138	17925/19	32/F	8450	85	13	1	1	0	8.5	26.7	72.3	23	31.8	396000	15.1	5240	6	1098.5	360	1	S	OP	S
139	17215/19	20/M	9330	78.2	17.8	0.1	3.6	0.3	15.9	44.3	82.2	29.5	35.9	166000	12.2	6080	4	1660.74	99	1	S	OP	S
140	16138/19	60/M	8730	83.3	12	0.5	4.1	0.1	11.7	33.4	97.1	34	35	93000	13	3860	6	1047.6	88	2	S	OP	S
141	16463/19	24/F	8070	85.6	10.9	0.1	3.3	0.1	10.7	18.2	91.3	34.6	37.9	168000	14.9	4010	7	879.63	190	2	S	OP	S
142	16408/19	24/F	9100	75.8	18.9	1.8	3.1	0.4	12.5	35.9	86.1	30	34.8	333000	12.3	7350	4	1719.9	193	1	S	OP	S
143	16577/19	24/M	19320	87.5	7.9	0.3	4.1	0.2	14	44.4	74.7	23.6	31.5	434000	13.3	430	11	1526.28	284	3	S	OP	S
144	16626/19	35/M	19230	92.8	3	0.1	3.8	0.3	16.7	47.2	80.3	28.4	35.4	259000	12.7	200	30	576.9	448	3	NS	OP	S
145	15798/19	22/F	11690	70.9	25.4	0.9	2.5	0.3	13.4	38.6	77.8	27	34.7	244000	16.7	6880	2	2969.26	82	1	S	OP	S
146	15792/19	28/F	11260	78.2	17.4	1.1	2.9	0.4	11.8	34.9	80.8	27.3	33.8	309000	13.4	5960	4	1959.24	157	1	S	OP	S
147	15899/19	45/F	10290	77.1	16.6	2.8	2.6	0.9	11.8	35.5	92.6	30.7	33.1	214000	15.8	5320	4	1708.14	125	1	S	OP	S
148	19160/19	26/F	10590	81.5	14.5	2.8	1	0.2	9.7	29.9	95.8	31.2	32.5	158000	17.6	4600	5	1535.55	102	1	S	OP	S