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Evaluate Theprognostic Value of Neutrophil Lymphocyte Ratio in Patient of Organo Phosphorous Poisoning

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Abstract – Organophosphorus is the commonest poisoning for harming in India. Neutrophil to lymphocyte proportion (NLR) is an easy and fundamental boundary that is promptly acquired from the total blood tally. In the creating scene, Poisoning is a typical technique for suicide. (1) Pesticide harming is a significant wellbeing danger in the creating scene. A large number of individuals are presented to these perilous synthetic compounds due to the word related dangers and furthermore on account of risky stockpiling rehearses. Nonetheless it is simply the conscious harming that prompts larger part of the passings and a troublesome wellbeing methodology to oversee among wellbeing administrations, particularly in Asia. (2) The world Health Organization (WHO) gauge that internationally 3,000,000 deliberate or unexpected pesticide poisoning happen every year and out of these at least 300,00 die. Organophosphorus (OP), the commonest poisoning in India because of its minimal expense and effectively availability.(3) The frequency of Organophosphorus poisoning in India was around 1.26 lakhs during the time of a year in 2007 as announced by Ravi et al.(4) 5 to 6 percent for each lakhs of populace pass on because of poisoning each year. The side effects are arranged into muscarinic, nicotinic and focal relying upon the site of the compound over the individual receptors. Urination, lacrimation, emesis, meiosis, unnecessary salivation, bradycardia, looseness of the bowels, and wheezing are the muscarinic symtoms. Nicotinic symptoms are paresis, fasciculation, tachycardia, and hypertension. Focal symptoms incorporates disarray, tension, seizures, ataxia and psychosis.

Keywords – Organophosphorus, Poisoning, Neutrophil-Lymphocyte Ratio (NLR), Marker.

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INTRODUCTION

Organophosphates (OPC) are additionally utilized in substance fighting. Albeit self-destructive harming is the most normally ascribed cause, incidental and surprisingly exposure can likewise happen.

Organophosphate engineered materials act by repressing acetyl cholinesterase (AChE), a compound hydrolyzing acetylcholine in cholinergic neurotransmitters and neuromuscular intersections, by phosphorylating it. They are along these lines called Ach Einhibitors. Inhibition of AChE causes collection of acetylcholine, with ensuing expanded movement of cholinergic muscarinic.

In instances of serious harming, indications of OPC harming happens normally inside 6 hours after exposure and are probably not going to happen if the uncovered individual remaining parts manifestation free for 12 hours post utilization. Despite the fact that their systems of activity are extraordinary, in practically all intense pesticide harming, an overall incendiary reaction happens in the body because of oxidative pressure. Because of this provocative reaction, significant research center irregularities, like leukocytosis and hyperglycemia, can be distinguished in patients with pesticide harming. At the point when the differential check of leukocytes is assessed during the intense provocative reaction to oxidative pressure, it is described by an increment in neutrophil tallies, an expansion in monocyte tallies, and a decrease in lymphocyte tallies. The proportion of neutrophil-lymphocyte likewise can be utilized as an extra incendiary marker.

HISTORY OF ORGANOPHOSPHORUS COMPOUNDS:

Early pioneers in the field incorporate Jean Louis Lssaigne (mid nineteenth century) and Philippe de Clermont (1854). In 1932, German physicist Willy Lange and his alumni understudy, Gerde von Krueger, first depicted the cholinergic sensory system impacts of organophosphates. The main OP, tetraethyl pyrophosphate (TEPP), was combined in

1854, yet the class was not effectively utilized financially until World War II when the Germans utilized TEPP as a substitute for the scant botanic bug spray nicotine. The human harmfulness of OPs was misused by the Germans toward the finish of World War II with the improvement of the nerve specialists' tabun, sarin, and soman (GA, GB, and GD).

CHEMICAL CLASSIFICATION OF REPRESENTATIVE ORGANOPHOSPHORUS COMPOUNDS:

Group A, X = halogen, cyanide, or thiocyanate leaving group; **group B**, X = alkylthio, arylthio, alkoxy, or aryloxy leaving group; **group C**, thionophosphorus or thio-thionophosphorus compounds; **group D**, pyrophosphates and similar compounds; **group E**, quaternary ammonium leaving group. R1 can be an alkyl (phosphonates), alkoxy (phosphorates) or an alkylamino (phosphoramidates) group.

CONSTRUCTION OF ORGANOPHOSPHATES:

Operations are a heterogeneous gathering of mixtures however share some normal substance properties. Operations contain a focal phosphorus molecule with a twofold cling to one or the other oxygen (P=O) or sulfur (P=S), two natural side chains (R1 and R2), and an extra side chain that turns into the leaving bunch (X). The leaving bunch is explicit to the individual OP and might be a cyanide, thiocyanate, halide, phosphate, phenoxy, thiophenoxy, or carboxylate bunch. The R1 and R2 bunches are aryl or alkyl gatherings and, in the vast majority of the normal pesticides, are either two methyl or two ethyl ester bunches that structure the dimethyl (dimethoxy) or diethyl (diethoxy) OPs.

Three sort of neuro strong loss of motion are taken note-

- Type 1 is because of proceeded with depolarization at neuro-solid intersection.
- Type 2 because of halfway disorder and
- Type 3 due to postponed polyneuropathy.

Neutrophil to lymphocyte proportion (NLR) is an easy and essential boundary that is promptly gotten from the total blood check, even in fringe medical clinics. Complete platelet tally is one of the easiest and most promptly accessible tests in the center, which reports the total neutrophil and lymphocyte checks. The serum neutrophil-to-lymphocyte proportion (NLR) is a conservative and helpful marker of foundational irritation.

Further examination in such manner may give a more complete perspective on ailment seriousness and a knowledge into expected etiology. Subsequently, this examination is attempted to evaluate neutrophil lymphocyte proportion (NLR) as a prognostic marker in understanding of Organo-phosphorus harming.

PATHOPHYSIOLOGY OF TOXICITY:

Organophosphates produce toxicity by binding to and inhibiting the action of acetyl cholinesterase at its serine active site. Acetylcholine accumulates at nerve terminals, initially stimulating, then paralyzing,simpler to perform, this is the more readily available assay in hospitals and in the field.

Acetyl cholinesterase is a convoluted protein structure with a pit containing a serine binding site and a catalytic site. Initially, the electrophilic OP oxon forms a reversible Michaelis-Menten complex, binding to the serine enzymatic active site followed by rapid phosphorylation of the serine residue. Once this happens, the leaving group (X) on the OP is released. As this reaction occurs, the OP becomes covalently bound to the enzyme, sitting in the pit and changing the conformation of the enzyme, preventing the active site from binding acetylcholine, and subsequently inhibiting catalytic activity. The organ phosphorylated enzyme can then undergo two different reactions. The enzyme can become “aged” or irreversibly bound and inactivated by cleavage of one of the R groups. This dealkylation process leads to a monosubstituted phosphoric acid residue that remains firmly attached to the enzyme. The rate of aging depends on the specific OP agent. Alternatively, reactivation of the enzyme can occur when the bond between the serine and organophosphorus moiety hydrolyzes. Enzyme reactivation occurs spontaneously at an extremely slow rate for diethyl-containing

Generally, the pharmacological properties of anti-ChE agents can be predicted by knowing those loci where ACh is released physiologically by nerve impulses, the degree of nerve impulse activity, and the responses of the corresponding effector organs to Ach. The anti-ChE agents potentially can produce all the following effects:

1. Stimulation of muscarinic receptor responses at autonomic effector organs;
2. Stimulation, followed by depression or paralysis, of all autonomic ganglia and skeletal muscle (nicotinic actions); and
3. Stimulation, with occasional subsequent depression, of cholinergic receptor sites in the CNS.

Following toxic or lethal doses of anti-ChE agents, most of these effects can be noted. However, with smaller doses, particularly those used therapeutically, several modifying factors are significant. In general, compounds containing a quaternary ammonium group do not penetrate cell

membranes readily; hence, anti-ChE agents in this category are absorbed poorly from the GI tract or across the skin andare excluded from the CNS by the blood–brain barrier after moderate doses. On the other hand, such compounds act preferentially at the neuromuscular junctions of skeletal muscle, exerting their action both as anti-ChE agents and as direct agonists. They have comparatively less effect at autonomic effector sites and ganglia. In contrast, the more lipid-soluble agents are well absorbed after oral administration, have ubiquitous effects at both peripheral and central cholinergic sites, and may be sequestered in lipids for long periods of time. Lipid-soluble organophosphorus agents also are well absorbed through the skin, and the volatile agents are transferred readily across the alveolar membrane.

OBJECTIVE

- To consider Neutrophil Lymphocyte Ratio in quiet with OP harming inside 24 hour of ingestion/inward breath/skin openness.
- To consider the Neutrophil Lymphocyte Ratio in age and sex coordinated with sound subjects.

RESEARCH METHODOLOGY

SOURCE OF DATA:

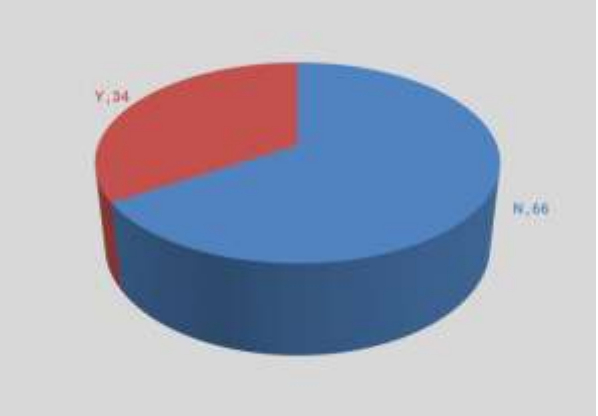
This is a cross sectional examination was directed subsequent to taking an educated assent from patients or their family members on 100 patients of OPC Poisoning who was conceded in Department of Medicine, J.L.N. Medical College and Associated Hospitals, Ajmer (Raj.) over a time of two years in the wake of acquiring moral panel endorsement. Patients of all ages >18 yrs.

All patients (≥18 years old) conceded to the loss from Oct 2018 through Apr 2020 because of OPC harming were taken on the examination. The composed clinical graphs of patients was looked into. Neutrophil-lymphocyte proportion was determined for every tolerant utilizing total neutrophils and lymphocyte tallies. Mechanical ventilation necessity and mortality were utilized as the essential endpoints.

Ventilator support

Ventilator support	Frequency	Percent
N	66	66.0
Y	34	34.0
Total	100	100.0

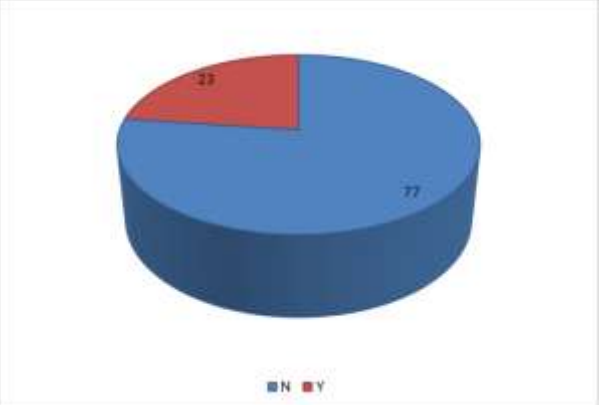
Ventilator support was needed for 34.00 per cent of the total population while rest 66.00 per cent didn't require any ventilator support.



Mortality

Mortality	Frequency	Percent
N	77	77.0
Y	23	23.0
Total	100	100.0

Mortality was reported in 23.00 per cent patients while it was not reported in rest 77.00 per cent.



TO ASSESS HEMATOLOGICAL PARAMETERS AND NLR

Maker and Instrument Name: Sysmex America, Inc. Sysmex XS Automated Hematology Analyzer series (XS-100i and XS-800i).

Kind of Test or Tests Performed: 21 Complete Blood Count examination boundaries in entire blood.

Framework Descriptions: 1. Gadget Description: The XS is a mechanized hematology analyzer which comprises of three head units:

- Primary unit which suctions, weakens, blends and examines entire blood tests;
- Auto Loader on the XS-1000i that provisions tests to the Main Unit naturally
- IPU (Information Processing Unit) which measures information from the Main Unit and

furnishes the administrator interface with the framework.

The XS-1000i and XS-800i are the very instruments aside from that the XS1000i can introduce an auto loader and the XS-800i utilizations a manual mode in particular. 2. Standards of Operation: The XS performs hematology examinations utilizing the accompanying techniques: Sheath Flow DC Detection Method, Flow Cytometry Methods utilizing a Semiconductor Laser and SLS-hemoglobin strategy.

Platelets go through the opening of the indicator encompassed by a sheath liquid utilizing the sheath stream strategy. The rule of stream cytometry is likewise utilized. A semiconductor laser bar is transmitted to the platelets going through the stream cell. The forward dispersed light is gotten by the photodiode, and the sidelong dissipated light and horizontal bright light are gotten by the photograph multiplier tube. This light is changed over into electrical heartbeats, along these lines making it conceivable to acquire platelet data. Hemoglobin is estimated with the SLS-hemoglobin technique utilizing Sodium Lauryl Sulfate, which is an investigation strategy utilized in past Sysmex instrumentation.

1. Methods of Operation: Sampler Mode, Capillary Mode, and Manual Mode with XS-1000i and Manual Mode and Capillary Mode with XS-800i.

2. Example Identification: Barcode just with XS-1000i when Sampler is associated.

3. Example Sampling and Handling: Sampler Mode, Capillary Mode, and Manual Mode with XS-1000i and Manual Mode and Capillary Mode with XS-800i

Every one of the boundaries were organized. Mean, Standard deviation were investigated utilizing SPSS 20 programming. Chi-square test was the trial of importance utilized for subjective factors to discover the relationship between them. T test was the trial of importance utilized for contrasting quantitative factors and subjective variable. Single direction Anova is utilized as trial of importance to evaluate different boundaries with the compound utilized for harming.

INCLUSION CRITERIA

All the OP harming cases affirmed by history, conditional proof of ingestion, inward breath and skin openness conceded in our emergency clinic inside 24 hours of ingestion with trademark clinical discoveries and fundamental research facility examinations were remembered for the investigation.

EXCLUSION CRITERIA

1. Patients with highlight of openness to another compound not identifying with OP Poison (for example carbamate).

2. Patients with blended harming; OP harming and some other toxin

3. Patients who has ongoing liquor abuse

4. Patients with history or clinical proof reminiscent of liver illness

5. History and clinical proof reminiscent of myopathy

6. Patients with history and clinical proof of danger and immune system sicknesses

7. Patients with history and clinical proof of renal sickness

8. Patients with history and clinical proof of heart illness

9. Patients with history and clinical proof of persistent smoking

10. Patients with history and clinical proof of blood dyscrasias

RESULT

Table 11:

WBC (cells/mm^3)

	Mean	Std. Dev	Minimum	Maximum	P value
Case	12715.59	3726.767	5700	25000	0.001 (S)
Control	6527.32	1113.846	3500	8976	

The WBC was found to be 12715.59 ± 3726.77cells/mm^{3}of blood, in case group and 6527.32 ± 1113.85cells/mm^{3}of blood, in control group. Both of these values were very significantly (P<0.01) different.

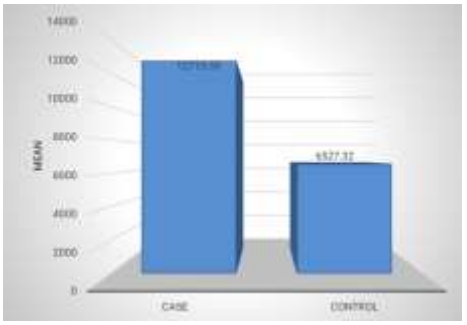


Figure9: WBC

Table 12: N/L RATIO

	Mean	Std. Dev	Minimum	Maximum	P value
Case	13.4551	7.38110	1.59	34.25	0.001 (S)
Control	7.8261	3.10976	3.23	16.04	

The N/L ratio was found to be 13.46 ± 7.38 in case group while it significantly (P<0.01) lower in control group (7.83 ± 3.11).

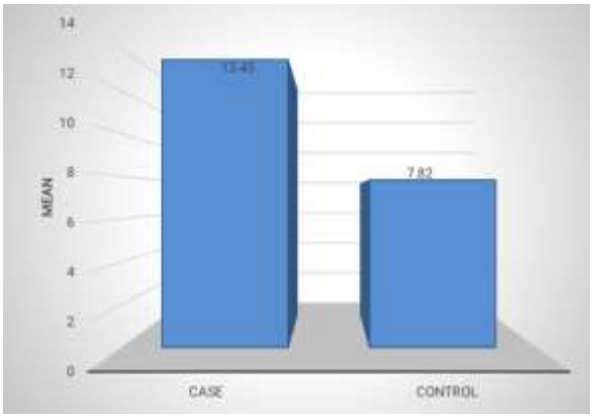


Figure10: N/L RATIO

Table 13: N/L ratio and Route of exposure

	N	Mean	Std. Deviation	P value
Inhalation	7	8.104	7.03	0.08
Oral	89	14.02	7.33	
Transdermal	4	10.25	5.61	

In inhalation, oral and transdermal route of exposure, N/L ratio was 8.10 ± 7.03, 14.02 ± 7.33 and 10.25 ± 5.61 respectively. There was not any significant difference between groups.

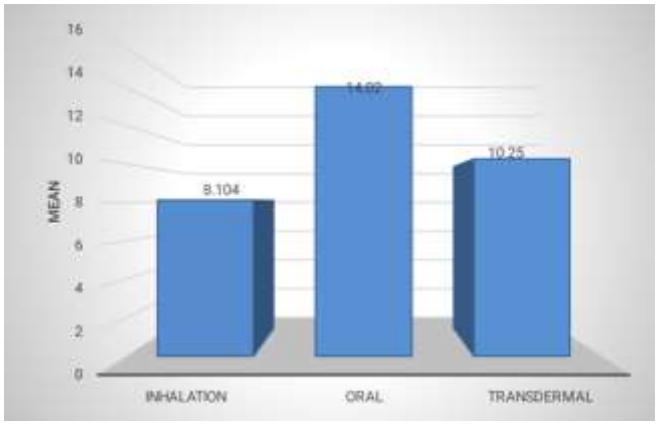


Figure 11: N/L ratio and Route of exposure

Table 14

N/L ratio and Manner of Poisoning

	N	Mean	Std. Deviation	P value
Accidental	22	11.66	6.13	0.19
Suicidal	78	13.95	7.65	

N/L ratio was 11.66 ± 6.13 in the patients who had accidental history while it was 13.95 ± 7.65 in the patients who had suicidal history. Both of these were not significantly different.

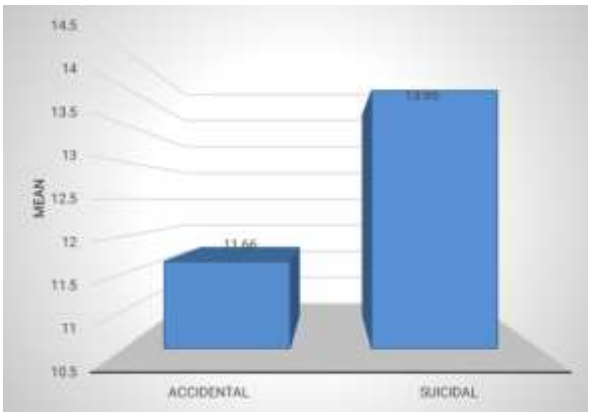


Figure 12: N/L ratio and Manner of Poisoning

Table 15: N/L ratio and Ventilator support

	N	Mean	Std. Deviation	P value
N	66	11.21	6.51	0.001 (S)
Y	34	17.79	7.09	

N/L ratio was 11.21 ± 6.51 in the patients who didn't need ventilator support and this was very significantly (P<0.01) lower in comparison to the patients who needed ventilator support (17.79 ± 7.09).

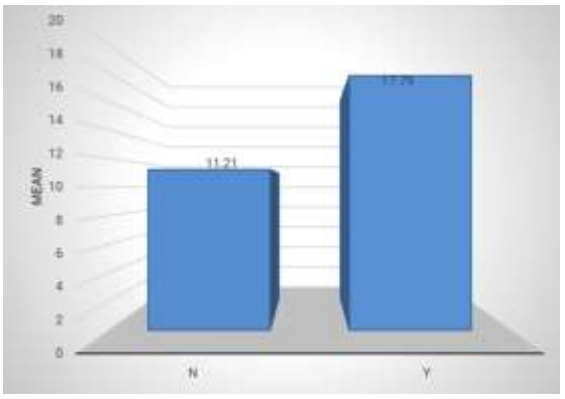
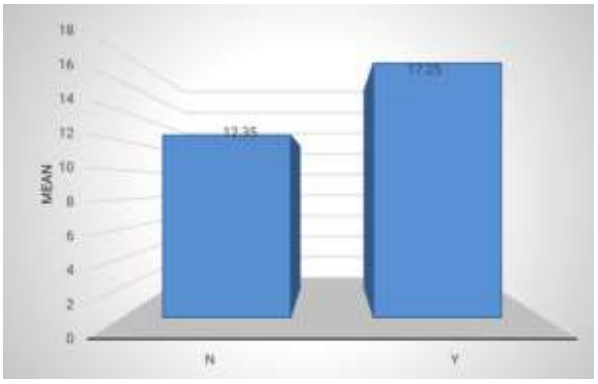


Figure 13: N/L ratio and Ventilator support

Table 16: N/L ration and mortality

	N	Mean	Std. Deviation	P value
N	77	12.35	7.14	0.006 (S)
Y	23	17.25	7.23	

N/L ratio was 12.35 ± 7.14 in the patients where mortality was reported and this was also found to be very significantly (P<0.01) lower in comparison to the patients where mortality was reported (17.25 ± 7.23).



Graph: 14 N/L ration and mortality

OPC poisoning is a major health hazard in the developing world.[2] Millions of people are exposed to these dangerous chemicals because of the occupational hazards and also because of unsafe storage practices.[31]Inhibition of acetyl cholinesterase is the main mechanism by which organophosphates act leading to excessive cholinergic stimulation. The clinical features of cholinergic storm develops fast, which helps in diagnosing clinically that is established by detailed history and biochemical demonstration of cholinesterase inhibition. This study is undertaken to analyzethe biochemical abnormalities in organophosphate poisoning and to assess their prognostic significance.

This is a cross sectional study which was conducted after taking an informed consent from patients or their relatives on patients of OPC Poisoning who were admitted in Department of Medicine, J.L.N. Medical College and Associated Hospitals, Ajmer (Raj.) over a period of two years after obtaining ethical committee approval. Patients of any age >18 yrs.

In the case group (patients with OPC poisoning), nausea, vomiting and excessive salivation were the most frequently found symptoms (100.00%, 78.00% and 58.00% respectively). Regarding signs of poisoning, miosis, bradycardia and fasciculation's were the most common signs (100.00%, 79.00% and 59.00% respectively).

CONCLUSION

This cross-sectional examination was led at J.L.N. clinical school on 100 patients of OPC harming to explore the prognostic worth of the neutrophil-lymphocyte proportion and to investigation of hematological boundaries estimated in patients with organo-phosphorus harming inside the initial 24 h after admission to the crisis office (ED). Two gatherings (the case and the control) were shaped with 100 subjects in each gathering. Here are the notable discoveries of this examination. Organophosphorus harming is more normal in grown-ups old enough gathering 20–30 years. OPC harming rates are high in male patients. Queasiness, spewing and inordinate salivation were the most as often as possible discovered side effects and miosis, bradycardia and fasciculation's were the most well-known indications of OPC harming. Chlorpyrifos 30%, chorpyrifos, monocrotophos, profenofos half and dimethoate 30% were the most normally utilized OPC. N/L proportion was not discovered to be related with sort of toxic substance. Prerequisite of ventilator support is high, when the patient on confirmation has a higher grade of inebriation clinically.This is a retrospective study in which we could not analyze the pesticide subgroups due to the low number of cases. We also could not objectively evaluate the reliability of the history given by the patients concerning the type and times of pesticide exposure. Therefore, the prognostic value of the neutrophil-lymphocyte ratios in OPC poisoning patients should be evaluated in large-scale prospective studies. Besides, serial estimation of the biochemical parameters during the course of hospital stay is not done. Previously undiagnosed cardiac disease is not ruled out in the study patients.

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