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FREQUENCY OF LEUKOCYTOSIS IN PATIENT PRESENTING WITH ORGANOPHOPHATE POISONING

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ABSTRACT

Background: Organophosphate (OP) poisoning is a major cause of acute pesticide toxicity and may produce substantial systemic physiological stress. Leukocytosis is a recognized response to acute stress and has been investigated as an accessible laboratory parameter in OP poisoning. This study assessed the frequency of leukocytosis among patients presenting with acute OP poisoning.

Objective: To determine the frequency of leukocytosis among patients presenting with organophosphate poisoning to the emergency department of a tertiary-care hospital.

Method: A cross-sectional study was conducted at the Department of Medicine, Abbasi Shaheed Hospital, Karachi, from January 18 to July 17, 2023. A total of 132 patients aged 16–65 years presenting within one hour of OP ingestion were enrolled through non-probability consecutive sampling. Patients with mixed or multiple poisoning, steroid use, immunocompromised status, or refusal of consent were excluded. After initial stabilization, demographic and clinical information was recorded, and a 5-mL blood sample was obtained for total leukocyte count (TLC). Leukocytosis was defined according to the study's operational definition. Data were analyzed using SPSS version 22. Continuous variables were assessed for normality using the Shapiro–Wilk test, while categorical variables were analyzed using the chi-square or Fisher's exact test. A p-value ≤0.05 was considered statistically significant.

Results: The mean age of participants was 30.89±11.50 years, and 87 (65.9%) were male. The mean TLC was 9.46±2.97 ×10⁹/L. Leukocytosis was present in 49 (37.1%) patients. No statistically significant association with leukocytosis was observed for age group (p=0.586), gender (p=0.103), residential status (p=0.586), marital status (p=0.531), educational status (p=0.173), diabetes mellitus (p=0.768), hypertension (p=0.310), or smoking status (p=0.835).

Conclusion: Leukocytosis was observed in more than one-third of patients with acute OP poisoning. Routine leukocyte assessment may provide a readily available indicator of the systemic response to poisoning, although its clinical significance and prognostic value require further investigation.

KEYWORDS: Organophosphate, Intoxication, Leukocytosis, Poisoning

1.INTRODUCTION

Organophosphate (OP) compounds are widely used insecticides in agricultural and domestic settings and remain an important cause of acute pesticide poisoning worldwide. Their widespread availability, relatively easy accessibility, and use in intentional self-poisoning contribute substantially to the global burden of pesticide-related morbidity and mortality [1,2]. Exposure may occur through ingestion, inhalation, or dermal absorption, while the clinical severity depends on the dose, route of exposure, duration of exposure, and characteristics of the specific compound involved [1,37]. Occupational exposure is also an important concern in agricultural communities, particularly where appropriate protective equipment, training, and safe pesticide-handling practices are inadequate [3,7,48]. In Pakistan, pesticide poisoning represents an important public health problem, and deliberate self-poisoning with pesticides is frequently encountered in hospital settings [3-5]. Organophosphorus poisoning may result in substantial morbidity and mortality, particularly in severe cases complicated by respiratory failure and cardiovascular complications [6,50]. Consequently, early recognition and appropriate assessment of patients with acute OP poisoning remain important components of emergency care.

The principal mechanism of acute OP toxicity is inhibition of acetylcholinesterase (AChE), resulting in accumulation of acetylcholine at cholinergic synapses [1,31,37]. Persistent cholinergic stimulation produces characteristic muscarinic, nicotinic, and central nervous system manifestations. Patients may develop excessive salivation and lacrimation, miosis, sweating, vomiting, diarrhea, bronchial secretions, fasciculations, muscle weakness, altered consciousness, seizures, and respiratory distress [1,37]. Severe poisoning may progress to respiratory failure, which is an important cause of death in patients with acute organophosphate and carbamate poisoning [50]. The intensity of the toxic response and associated

systemic physiological stress may also produce measurable changes in routine hematological parameters.
Leukocytosis is a common hematological response to acute physiological stress. It may result from redistribution and demargination of leukocytes into the circulating blood, particularly neutrophils, rather than an immediate increase in leukocyte production [8,13-15]. Acute stress activates sympathetic pathways and increases circulating catecholamines and glucocorticoids, which can contribute to transient elevations in leukocyte counts [13-15]. Toxic exposure, tissue injury, inflammation, medications, and associated physiological disturbances may further influence leukocyte concentrations [13-15]. Therefore, an elevated total leukocyte count may provide an accessible indicator of the systemic response occurring during acute poisoning, although leukocytosis is nonspecific and must be interpreted in conjunction with the clinical condition of the patient.
Several studies have investigated leukocyte abnormalities in acute OP poisoning. Kumar et al. reported leukocytosis in 32.5% of patients with organophosphate poisoning and suggested that leukocyte count may provide information regarding the severity of intoxication [9]. Cander et al. evaluated leukocyte levels together with the Glasgow Coma Scale and serum acetylcholinesterase and reported that these parameters may have prognostic relevance in acute organophosphorus poisoning [10]. Leukocyte abnormalities have also been described among laboratory findings in patients presenting with acute suicidal organophosphate poisoning [12]. These observations indicate that leukocytosis may accompany acute OP toxicity and potentially reflect the magnitude of the systemic physiological response.
The relationship between pesticide exposure and systemic biological effects is complex. Organophosphate toxicity can involve neurological, respiratory, and other systemic effects, and both acute and repeated exposure may produce clinically important consequences [36,41,42]. Biomarkers of susceptibility, including paraoxonase-1 activity, have also been investigated in relation to organophosphate toxicity [33]. However, such specialized investigations are not routinely available in many emergency departments. In contrast, a complete blood count is inexpensive, widely available, and routinely performed, making leukocyte count a practical parameter for evaluating patients with acute poisoning.
Interpretation of leukocytosis nevertheless requires attention to timing and potential confounding factors. Leukocyte elevation may occur because of infection, tissue injury, medications, or other stress-related conditions [13-15]. Reference intervals may also vary according to population characteristics and demographic factors [21]. Consequently, documenting leukocytosis specifically at presentation may help distinguish the hematological response associated with acute poisoning from abnormalities developing later during hospitalization.
Despite evidence from international studies, limited local data are available regarding the frequency of leukocytosis among patients presenting with acute OP poisoning in Pakistan. Differences in pesticide exposure patterns, intentional and occupational exposure, patient characteristics, healthcare access, and clinical management may influence the observed hematological response [3-6]. The present study was therefore conducted to determine the frequency of leukocytosis among patients presenting with organophosphate poisoning to the emergency department of a tertiary-care hospital. The findings may provide locally relevant evidence regarding the hematological response to acute OP poisoning and contribute to its clinical assessment.

2. METHODOLOGY

This was a cross-sectional study conducted at the Department of Medicine, Abbasi Shaheed Hospital, Karachi. The study was conducted over a period of six months after approval of the synopsis, from January 18, 2023, to July 17, 2023. The sample size was calculated using the WHO sample size calculator, based on a reported frequency of leukocytosis in patients with organophosphate poisoning of 32.5%, a margin of error of 8%, and a 95% confidence level. The required sample size was 132 participants. A non-probability consecutive sampling technique was used. Patients aged 16–65 years of either gender who presented with organophosphate poisoning within one hour of ingestion were eligible for inclusion. Patients with double insecticide poisoning or multiple poisoning involving other drugs, such as opioids, diazepam, or alcohol, were excluded. Non-consenting patients or attendants, patients with a history of steroid use, and immunocompromised patients were also excluded.

2.1 Data Collection

The study was started after taking approval from CPSP and the ethical review board of the institute. All patients presented in an emergency department with organophosphate poisoning and fulfilling the inclusion criteria were enrolled in the study. Before enrollment, complete details of the study were explained to the patient attendants and written informed consent was taken. After stabilizing the patient, baseline clinical and demographic details were taken at the time of presentation in an emergency department and noted in a predesigned Performa. A 5cc blood sample was taken by the phlebotomist using an aseptic technique and sent to the laboratory for the TLC count. Based on TLC, leukocytosis was labelled as per the operational definition. All patients with organophosphate poisoning were managed as per hospital protocol. All the findings of study variables such as age, gender, residence, marital status, education, diabetes (known h/o 6 months), hypertension (known h/o 6 months), smoking (smoked 5 or more cigarettes/day for last 1 year) and leukocytosis was noted in a predesigned proforma.

2.2 Data Analysis

The data was analyzed using SPSS version 22. The normality of the continuous data was tested by the Shapiro-Wilk test. Mean and standard deviation or median (IQR) was reported on the basis of normality for quantitative variables such as age, total leukocyte count and duration of poison ingestion. While frequency and percentage were reported for qualitative variables such as gender, residence, marital status, educational status, diabetes mellitus, hypertension, smoking status and leukocytosis. Effect modifiers such as age, gender, residential status, marital status, educational status, diabetes mellitus, hypertension and smoking status were controlled through stratification. Post-stratification, an appropriate Chi-square/Fischer Exact test was applied taking p-value ≤ 0.05 as significant.

3. RESULTS

A total of 132 patients presenting with organophosphate poisoning to the emergency department of a tertiary care hospital were included in the study. The distribution of continuous variables was assessed using the Shapiro–Wilk test. Age (P=0.063), total leukocyte count (P=0.078), and duration of poison ingestion (P=0.093) showed no significant departure from normality (Table 1).

The mean age of the patients was 30.89±11.50 years (95% CI: 28.91–32.87), with a median of 27.50 years and a range of 16–65 years. The mean total leukocyte count was 9.46±2.97 ×10⁹/L (95% CI: 8.95–9.98), with a median of 9.00 ×10⁹/L and a range of 5.0–15.0 ×10⁹/L. The mean duration from poison ingestion to presentation was 32.33±12.32 minutes (95% CI: 30.21–34.46), with a median of 31.50 minutes and a range of 10–55 minutes (Table 1).

Among the 132 patients, 87 (65.9%) were male and 45 (34.1%) were female (Figure 1). Regarding residential status, 90 (68.2%) patients were from urban areas and 42 (31.8%) were from rural areas (Figure 2).

With respect to marital status, 34 (25.8%) patients were single, 65 (49.2%) were married, 7 (5.3%) were widowed, 15 (11.4%) were separated, and 11 (8.3%) were divorced (Table 2). Regarding educational status, 12 (9.1%) patients were illiterate, 24 (18.2%) had primary education, 48 (36.4%) had secondary education, 17 (12.9%) had completed matriculation, 15 (11.4%) had intermediate education, and 16 (12.1%) were graduates (Table 2).

Diabetes mellitus was documented in 37 (28.0%) patients (Figure 3), while hypertension was present in 76 (57.6%) patients (Figure 4). Fifty (37.9%) patients were smokers, whereas 82 (62.1%) were non-smokers (Figure 5).

Leukocytosis was identified in 49 (37.1%) patients (Figure 6). Stratification was subsequently performed to assess the association between leukocytosis and age group, gender, residential status, marital status, educational status, diabetes mellitus, hypertension, and smoking status (Tables 3–10).

There was no statistically significant association between leukocytosis and age group (P=0.586), gender (P=0.103), residential status (P=0.586), marital status (P=0.531), educational status (P=0.173), diabetes mellitus (P=0.768), hypertension (P=0.310), or smoking status (P=0.835). Chi-square tests were applied for these comparisons.

Table 1: Distribution and descriptive statistics of continuous variables (n=132)

Variable	Mean±SD	95% CI	Median	Range	Shapiro–Wilk P-value
Age (years)	30.89±11.50	28.91–32.87	27.50	16–65	0.063
Total leukocyte count (×10⁹/L)	9.46±2.97	8.95–9.98	9.00	5.0–15.0	0.078
Duration of poison ingestion (min)	32.33±12.32	30.21–34.46	31.50	10–55	0.093

Table 2: Frequency distribution of marital and educational status (n=132)

Variable	Category	n (%)
Marital status	Single	34 (25.8)
	Married	65 (49.2)
	Widowed	7 (5.3)
	Separated	15 (11.4)
	Divorced	11 (8.3)
Educational status	Illiterate	12 (9.1)
	Primary	24 (18.2)
	Secondary	48 (36.4)
	Matric	17 (12.9)
	Intermediate	15 (11.4)
	Graduate	16 (12.1)

Figure 1: Frequency distribution of gender among patients with organophosphate poisoning (n=132)

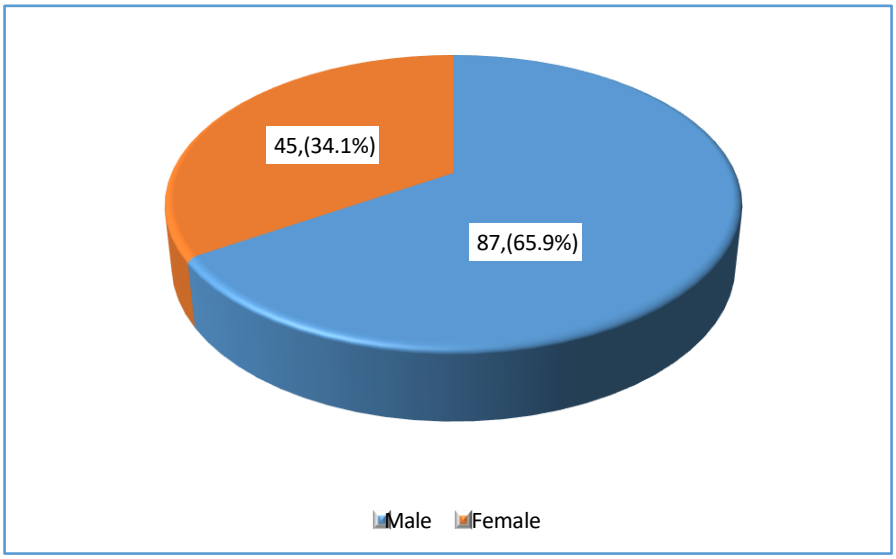


Figure 2. Frequency distribution of residential status among patients with organophosphate poisoning (n=132)

Table 3. Association between age group and leukocytosis (n=132)

Age group (years)	Leukocytosis, n (%)	No leukocytosis, n (%)	P-value
16–30	33 (25.0)	52 (39.4)	0.586
>30	16 (12.1)	31 (23.5)	
Test applied	Chi-square test		

Table 4. Association between gender and leukocytosis (n=132)

Gender	Leukocytosis, n (%)	No leukocytosis, n (%)	P-value
Male	28 (21.2)	59 (44.7)	0.103
Female	21 (15.9)	24 (18.2)	
Test applied	Chi-square test		

Table 5. Association between residential status and leukocytosis (n=132)

Residential status	Leukocytosis, n (%)	No leukocytosis, n (%)	P-value
Urban	32 (24.2)	58 (43.9)	0.586
Rural	17 (12.9)	25 (18.9)	
Test applied	Chi-square test		

Table 6. Association between marital status and leukocytosis (n=132)

Marital status	Leukocytosis, n (%)	No leukocytosis, n (%)	P-value
Single	10 (7.6)	24 (18.2)	0.531
Married	27 (20.5)	38 (28.8)	
Widowed	4 (3.0)	3 (2.3)	
Separated	5 (3.8)	10 (7.6)	
Divorced	3 (2.3)	8 (6.1)	
Test applied	Chi-square test		

Table 7. Association between educational status and leukocytosis (n=132)

Educational status	Leukocytosis, n (%)	No leukocytosis, n (%)	P-value
Illiterate	6 (4.5)	6 (4.5)	0.173
Primary	10 (7.6)	14 (10.6)	
Secondary	17 (12.9)	31 (23.5)	
Matric	5 (3.8)	12 (9.1)	
Intermediate	2 (1.5)	13 (9.8)	
Graduate	9 (6.8)	7 (5.3)	
Test applied	Chi-square test		

Table 8. Association between diabetes mellitus and leukocytosis (n=132)

Diabetes mellitus		Leukocytosis, n (%)	No leukocytosis, n (%)	P-value
Diabetic		13 (9.8)	24 (18.2)	0.768
Non-diabetic	36 (27.3)	59 (44.7)		
Test applied	Chi-square test			

Figure 3. Frequency distribution of diabetes mellitus among patients with organophosphate poisoning (n=132)
Figure 4. Frequency distribution of hypertension among patients with organophosphate poisoning (n=132)
Figure 5. Frequency distribution of smoking status among patients with organophosphate poisoning (n=132)

Table 9. Association between hypertension and leukocytosis (n=132)

Hypertension	Leukocytosis, n (%)	No leukocytosis, n (%)	P-value
Hypertensive	31 (23.5)	45 (34.1)	0.310
Non-hypertensive	18 (13.6)	38 (28.8)	
Test applied	Chi-square test		

Table 10. Association between smoking status and leukocytosis (n=132)

Smoking status	Leukocytosis, n (%)	No leukocytosis, n (%)	P-value
Smoker	18 (13.6)	32 (24.2)	0.835
Non-smoker	31 (23.5)	51 (38.6)	
Test applied	Chi-square test		

4. DISCUSSION

Poisoning with organophosphorus (OP) compounds is an important global health problem having more concern in India. This region is home to approximately 3.4 million cotton farmers, and 95% of these are struggling with massive debt. The majority of poisoning cases are from agricultural areas due to the easy availability of OP compounds combined with their sale over the counter [35,45]. Laboratory evidence of OPP is usually confirmed by measuring the decreases in acetylcholine esterase activity [1,6,10,31,34].

Leukocytosis in stress like injury and poisoning is due to neutrophilia caused by neutrophil margination, and not due to increased marrow production. Normally, they are produced in the bone marrow and comprise approximately 60% of the blood. These cells are critically important to an immune response and migrate from the blood to tissues during infection and stress-like poisoning. Theoretically, patients with significant stress should have a higher degree of leukocytosis compared to patients with minor stress [8,13-15]. Since the complete blood count is one of the most common tests obtained in Intensive Care Unit (ICU) patients, leukocytes level could serve as an easy-to-obtain marker for the severity of organophosphorus poisoning (OPP). In centers where the measurement of cholinesterase activity cannot be done, management is based on the assessment of severity of intoxication, which depends largely on clinical findings and basic blood parameters such as leukocyte count [9,10,12,13,23].

Organophosphate compounds are frequently used as pesticides in countries that have a great deal of agricultural activities. OP poisonings are often encountered in Turkey as it is an agricultural country [47]. It has been reported in a statistical assessment conducted in the USA in 2003 that 18 out of every 100 000 agricultural laborers are exposed to pesticide-associated poisoning, and a total of 7500 OP poisonings occur annually [48]. Occupational and environmental exposure to organophosphorus pesticides has also been documented in agricultural and industrial workers and children, demonstrating the broad population exposure associated with pesticide use [38,43,48].

OP compounds increase the accumulation of acetylcholine in the synaptic gap through inhibition of acetylcholinesterase and decrease in the degradation of acetylcholine, thus leading to excessively increased cholinergic activity and the appearance of cholinergic symptoms [1,31,37]. Oximes like pralidoxime cause acetylcholinesterases to reactivate by binding to OP and carbamates that have been bound to acetylcholinesterases [44,49]. Since penetration of oximes into the central nervous system is limited, the actual effect is on the peripheral nervous system. OPs are quickly absorbed through the respiratory system, gastrointestinal system and mucosa, and they can be absorbed quickly from the skin as they are lipophilic compounds [1,34,37]. The severity of OP poisoning differs depending upon the compound and its quantity, the way the exposure has occurred and the time at which treatment is initiated [1,37,44]. Pesticide poisonings have a low mortality rate (0.04% to 1%) as long as they are treated appropriately; and the major reason for death is respiratory insufficiency [50,51]. OPs lead to undesired effects on the central nervous system, cardiovascular system, respiratory system, urogenital system, neuromuscular junction, and metabolic and endocrine systems [36,41,42]. Muscarinic symptoms like miosis, bradycardia, bronchospasm, urine and fecal incontinence; and nicotinic symptoms like muscle weakness, muscle fasciculations, tachycardia, loss of consciousness and globe vesicale occur [52,53].

OP and carbamate compounds are used commonly in agricultural countries, and they have been used for military purposes (including terrorist attacks) and for treatment of diseases like myasthenia gravis. OP poisonings can present to the emergency services with several clinical symptoms, and although they progress quickly and can be mortal, many are of a moderate exposure and symptoms generally disappear quickly. OP exposure can occur as a suicide attempt or as an accident [1,2,3,4,5]. The absorption of OP compounds differs according to the route of exposure. While the symptoms after oral intake begin in hours, they develop more quickly when exposure occurs through inhalation [52]. Repeated or low-level

exposure has also been associated with neurological and reproductive effects, although these effects differ from the acute clinical presentation considered in the present study [39-42].

The findings of our study are comparable with multiple studies conducted worldwide.

In this study, the mean age was 30.89±11.50 years. Another study found the mean age to be 33.52 years [9]. The study of Cander B, et al noted mean age of 37.8 years [10].

In our study, 87 (65.9%) were male while 45 (34.1%) were female. Kumar S, et al reported to have 71.25% of males and 28.75% of females [9] whereas Cander B, et al documented 48% of males and 52% of females [10].

In this study, leukocytosis was noted in 49 (37.1%) patients. A study by Kumar S, et al reported the prevalence of leukocytosis in patients with organophosphate poisoning was 32.5% [9]. Another study noted the prevalence of leukocytosis in patients with organophosphate poisoning was 76% [10]. The variability in leukocyte response may be related to differences in the severity of poisoning, timing of laboratory assessment, exposure characteristics, and other physiological or inflammatory factors [9,10,13-15]. Leukocyte count has therefore been investigated as a potentially accessible marker of disease severity, although it remains a nonspecific laboratory parameter [9,10,13,14].

In my study, stratification of confounders/effect modifiers with respect to leukocytosis, the insignificant difference was noted in age group (P=0.586), gender (P=0.103), residential status (P=0.586), marital status (P=0.531), educational status (P=0.173), diabetes mellitus (P=0.768), hypertension (P=0.310) and smoking status (P=0.835).

5. CONCLUSION

It is to be concluded that leukocytosis was commonly prevalent in patients presenting with organophosphate poisoning. Patients with organophosphate poisoning should be worked up for the presence of leukocytosis to ensure adequate treatment. Further large-scale work is recommended for the validation of current findings.

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