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Predictive Factors Influencing Length of Hospital Stay in Patients with Thrombocytopenia Following Pesticide Poisoning: A Retrospective Analysis

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Abstract

Background: Acute pesticide poisoning, particularly from suicide attempts or accidental exposure, is a growing issue, especially in developing countries. This study explores predictive factors for the Length of Stay (LOS) in patients with pesticide-induced thrombocytopenia.

Methods: This cross-sectional retrospective study was conducted at Khorshid Hospital, Isfahan University of Medical Sciences. It included patients aged 18 or older admitted between 2020 and 2021 with acute pesticide intoxication who experienced thrombocytopenia upon admission or during hospitalization, excluding those with significant pre-existing hematological conditions or a history anti-platelet medication. Data was collected on demographics, toxicological features, clinical and laboratory findings, and LOS. Data were extracted from patients' clinical records.

Results: Among the 240 patients studied, the average age was 36.3 years, with a majority being male. Most patients had an LOS of over 72 hours. Significant factors of longer LOS included the type of pesticide (with herbicides and fungicides associated with extended stays), higher white blood cell counts, and lower magnesium levels. There was no significant association between LOS and clinical outcomes. Multivariable linear regression revealed that benzodiazepine administration, and magnesium were associated with reductions in LOS and ICU admission, endotracheal intubation was associated with a longer length of stay ($p<0.05$).

Conclusion: The findings of this study suggest that targeted treatment with benzodiazepine may reduce hospital LOS. Additionally, monitoring of laboratory data such as WBC and magnesium level could also influence LOS. Future multicenter studies with larger sample sizes are necessary to further evaluate the predictive factors of LOS in these patients.

Keywords: Hospitals, Length of stay, Pesticides, Thrombocytopenia

Introduction

Pesticides are chemical products used to eradicate various pests and enhance agricultural efficiency (1). They include a wide range of substances such as insecticides, fungicides, herbicides, and rodenticides, which are used globally (2). The use of pesticides has increased significantly over recent decades, particularly in developing countries (3). Pesticides are widely used in Iranian agriculture which has become major toxicological concern among health professionals (4).

Acute pesticide poisoning is an emerging health issue in many countries, especially in developing nations such as Iran (5). Various studies have demonstrated the adverse effects of pesticides on human health (6). Despite their critical role in food supply, pesticides can impact different organs and cause serious illnesses (7). In addition to long-term effects, short-term exposure to pesticides can also lead to complications (8). Many other hematologic changes secondary to acute and chronic pesticide exposure have been documented in both humans and animals, although there are some conflicting results (9). Recent studies have shown that exposure to certain chemicals can result in changes to various hematological parameters. Specifically, there have been decreases in Red Blood Cell (RBC) and White Blood Cell (WBC) counts observed in cases of acute and chronic intoxications (10).

A review of case reports from 1946 to 1960 indicated that exposure to organochlorines, in particular, can lead to blood dyscrasias. However, it is uncertain whether this relationship is causal (11). Studies have demonstrated that Organochlorine Pesticides (OCPs) can impact the hematopoietic system through immunological mechanisms, potentially causing blood-related disorders (12). As fat plays a crucial role in supporting hematopoiesis, the accumulation of OCPs in bone marrow adipose tissue may elevate the risk of interfering with lymphohematopoietic function (13). Regarding the platelet levels, findings have been inconsistent and controversial, with reports of both thrombocytosis and thrombocytopenia in cases of pesticide exposure (14-19). The mechanism behind drug-induced thrombocytopenia is either a decrease in platelet production (bone marrow toxicity) or an increase in destruction (immune-mediated thrombocytopenia) (20).

Due to the fact that all the admitted patients experienced thrombocytopenia either upon admission or during hospitalization, it has been proposed that the Length of Stay (LOS) can greatly influence the development of thrombocytopenia in the admitted patients.

LOS defined as the duration a patient remains hospitalized, is a key indicator of patient outcomes. LOS can be influenced by various factors, including past medical history, disease severity, and type of medical interventions (21). However, the predictive factors for LOS in thrombocytopenic patients due to pesticide intoxication have not been thoroughly assessed. This current retrospective cross-sectional study aims to evaluate the predictive factors affecting LOS in patients with pesticide-induced thrombocytopenia.

Materials and Methods

This cross-sectional retrospective study was conducted at Khorshid Hospital, affiliated with Isfahan University of Medical Sciences, in Isfahan, Iran. The study adhered to the Declaration of Helsinki on biomedical ethics. Ethical approval was obtained from the Ethics Committee under code IR.MUI.MED.REC.1400.381.

In unpublished data from the center 240 patients with acute pesticide poisoning, who had no history of platelet abnormalities, experienced thrombocytopenia either upon admission or during hospitalization.

All the patients aged 18 or older were admitted to the referral poisoning center of Khurshid Hospital due to acute pesticide intoxication from 2020 to 2021 who experienced thrombocytopenia during hospitalization and were included in the current study. Inclusion criteria required no prior history of hematological conditions (especially coagulopathies or other platelet disorders), no history of anti-platelet medication before hospitalization and no somatic disease in the previous weeks.

Patients with incomplete data in their medical records or discharged due to personal consent or other non-medical reasons leading to early discharge were excluded.

Data collection

Data were collected using a data gathering form comprising various sections: demographics,

toxicological features, clinical and laboratory findings, and clinical measurements. The demographic section included variables such as age, sex, place of residence, education level, and marital status, season of toxicity and place of intoxication. The toxicological section covered the type of pesticide, route of poisoning, and the time interval between poisoning and hospitalization. Clinical and laboratory findings included vital signs, lab tests including CBC (WBC, RBC, HB, HCT, PLT), BUN, Cr, LFT (AST, ALT, ALP, total and direct bilirubin), BS, electrolytes (Na, K, Ca, phosphorus, Mg), coagulation tests (PTT, PT, INR), and clinical outcomes, including length of stay and indication for intubation or dialysis were recorded. All the protocol treatments were recorded.

Data were extracted from patients' clinical records. Two researchers collected the data under the supervision of an attending toxicologist. Diagnosis of intoxication was made by expert attending physicians based on clinical examination, vital signs, self-reported history or information from relatives, and clinical laboratory tests or urinary toxicological analysis when necessary.

Definitions

Pesticide intoxication is defined as any intentional or unintentional exposure to insecticides, herbicides, rodenticides, or other pesticides, regardless of clinical manifestations. Thrombocytopenia is defined as a platelet count of less than 150,000/μL in a Complete Blood Count (CBC) result upon admission. The patients were categorized into three groups based on their length of hospital stay: less than 24 *hrs*, 24-72 *hrs*, and more than 72 *hrs*. The severity of manifestations varies with the degree of poisoning (22).

Statistical analysis

SPSS 26 (IBM Corp., Armonk, NY, USA) was used for statistical analysis. Continuous variables were described by mean and standard deviation, while the categorical variables were described by frequency and percentage. Chi-square or Fisher exact tests were used for categorical data to assess between-group differences. Independent samples test and analysis of variance (ANOVA) were used for normally distributed continuous variables to assess between-group differences. Linear regression was used to evaluate the factors influencing the length of stay. Protocol treatments were categorized for linear regression as: Antidotes (pralidoxime, atropine), Antiapoptotic agents (vitamin C, vitamin E, corticosteroids) and Benzodiazepines (diazepam, midazolam) and antiacid (ranitidine, pantoprazole).

Results

A total of 240 patients were assessed in this study. The most frequently encountered pesticides among patients were insecticides (n=100), herbicides (n=57), rodenticides (n=66) and others (n=12), respectively. The mean age of the patients was 36.3±16.78 years. The gender distribution revealed a higher frequency of male patients, with 186 (77.5 %) males. The patients were categorized into three groups based on their length of stay. The majority of patients (123, 53.1%) were in the group with a stay of more than 72 *hrs*. Table 1 presents the toxico-epidemiologic characteristics and medical history of patients categorized by length of stay. There was a significant difference between the three groups in terms of types of pesticides. Patients in the herbicide and fungicide groups experienced longer hospitalizations. However, there were no significant differences between groups regarding other toxico-epidemiologic and demographic variables. There were also no significant differences between groups concerning physical illnesses, psychiatric disorders, or self-harm history. However, it is also worth noting that there were significantly higher frequencies of prolonged hospitalization among the patients with severe toxicity.

Results are expressed as numbers (percentages) or mean±standard deviation (SD). Categorical variables were analyzed between groups using Fisher's exact test or Chi-square test. *According to the post hoc analysis, a significant difference was observed between group 3 (more than 72 hours) and other groups

Therapeutic interventions and clinical outcomes were also compared between groups as shown in table 2. Patients with longer lengths of stay exhibited a higher frequency of requiring various treatments, including dialysis, ICU hospitalization, and intubation. Additionally, medications such as pralidoxime, atropine, NAC, vitamin C, vitamin E, Corticosteroids, pantoprazole, and KCl were significantly more

Table 1. The comparison of toxico-epidemiologic and medical history variables between groups based on the length of stay

Variables		Less than 24 hours N=34	24-72 hours N=21	Over 72 hours N=51	p-value
Age years (mean±SD)		35.02±60	36.77±17.79	36.72±17.55	0.79
Sex	Male	42(22.6%)	46(24.7%)	98(52.7%)	0.27
	Female	18(33.3%)	11(20.4%)	25(46.3%)	
Marriage status	Single	18(25.3%)	19(26.8%)	34(47.9%)	0.66
	Married	42(25.1%)	38(22.8%)	87(52.1%)	
	Widowed/Separated	0(0.0%)	0(0.0%)	2(100%)	
Place of habitancy	Isfahan city	26(27.7%)	24(25.5%)	44(46.8%)	0.26
	Isfahan province counties	34(24.6%)	32(23.2%)	72(52.2%)	
	Other provinces	0(0.0%)	1(12.5%)	7(87.5%)	
Education level	Illiterate	3(17.7%)	4(23.5%)	10(58.8%)	0.07
	Primary school	3(25%)	0(0%)	9(75%)	
	Junior high school	2(8.3%)	4(16.7%)	18(75%)	
	Diploma	8(23.5%)	15(44.1%)	11(32.4%)	
	Associate degree	1(33.3%)	1(33.3%)	1(33.3%)	
	Bachelor of science or higher degrees	1(11.1%)	3(33.3%)	5(55.6%)	
	Unknown	40(29.4%)	29(21.3%)	67(49.2%)	
Place of intoxication	Home	26(21.3%)	34(27.7%)	62(50.8%)	0.42
	At work	5(29.4%)	1(5.9%)	11(64.8%)	
	Other	10(28.5%)	6(17.1%)	19(54.3%)	
	Unknown	19(28.8%)	16(28.2%)	31(47%)	
Route of intoxication	Oral	56(24.3%)	55(23.8%)	120(51.9%)	0.19
	Inhaled	3(75%)	0(0.0%)	1(25%)	
	Injected	1(25%)	1(25%)	2(50%)	
	Unknown	0(0.0%)	1(100%)	0(0.0%)	
Season of poisoning	Spring	17(53.3%)	23(31.1%)	35(46.6%)	0.52
	Summer	16(30.3%)	13(24.5%)	25(47.2%)	
	Fall	12(21.1%)	11(19.3%)	34(59.6%)	
	Winter	15(27.8%)	10(18.5%)	29(53.7%)	
Pesticide type	Insecticides	32(31.3%)	18(17.6%)	52(51.1%)	<0.001*
	Herbicides and fungicide	5(8.5%)	10(16.9%)	44(74.6%)	
	Rodenticides	19(28.4%)	26(38.8%)	22(32.8%)	
	Other	4(33.3%)	3(25%)	5(41.7%)	
Addiction history	Yes	20(24.4%)	22(26.8%)	40(48.8%)	0.72
	No	40(25.3%)	35(22.1%)	83(52.6%)	
Mental illness history	Yes	11(20.7%)	15(28.3%)	27(51%)	0.58
	No	49(26.2%)	42(22.5%)	96(51.3%)	
Suicide history	Yes	9(23.1%)	14(35.9%)	16(41%)	0.14
	No	51(25.4%)	43(21.4%)	107(53.3%)	
Criminal history	Yes	4(44.4%)	3(33.3%)	2(22.2%)	0.19
	No	56(24.2%)	54(23.4%)	121(52.4%)	
Self-harm history	Yes	4(23.5%)	7(41.2%)	6(35.3%)	0.20
	No	56(25.1%)	50(22.4%)	117(52.5%)	

Contd. table 1.

Physical illness	Diabetes	0(0.0%)	1(100%)	0(0%)	0.60
	Nephrological disease	0(0.0%)	1(33.3%)	2(66.7%)	
	HTN or cardiologic diseases	1(12.5%)	2(25%)	5(62.5%)	
	Pulmonary diseases	1(100%)	0(0%)	0(0%)	
	Other diseases	6(28.6%)	6(28.6%)	9(42.8%)	
	Combined	5(27.8%)	6(33.3%)	7(38.9%)	
	No PMH	47(25%)	41(21.8%)	100(53.2%)	
Toxicity severity	Mild	48(28.2%)	48(28.2%)	74(43.4%)	0.003*
	Moderate	7(23.3%)	2(6.7%)	21(70%)	
	Severe	5(12.5%)	7(17.5%)	28(70%)	
The time between consuming the toxins and hospital admission(*h*) (mean±SD)		2.07±2.13	2.68±3.20	3.47±10.00	0.67

Results are expressed as numbers (percentages) or mean±standard deviation (SD). Categorical variables were analyzed between groups using Fisher's exact test or Chi-square test. *According to the post hoc analysis, a significant difference was observed between group 3 (more than 72 hours) and other groups.

Table 2. The comparison of therapeutic measures and outcomes between groups based on Length Of Stay (LOS)

Variables		Less than 24 hours	24-72 hours	Over 72 hours	p-value
Gastric lavage	Yes	39(27.3%)	30(21%)	74(51.7%)	0.39
	No	21(21.6%)	27(27.8%)	49(50.6%)	
Charcoal therapy	Yes	40(26.7%)	30(20%)	80(53.3%)	0.21
	No	20(22.3%)	27(30%)	43(47.7%)	
Pralidoxime	Yes	3(4.4%)	16(23.9%)	48(71.6%)	< 0.001*
	No	57(32.9%)	41(23.8%)	75(43.3%)	
Atropine	Yes	9(11.8%)	14(18.4%)	53(69.7%)	< 0.001*
	No	51(31.1%)	43(26.2%)	70(42.7%)	
NAC	Yes	15(12.3%)	31(25.4%)	76(62.3%)	< 0.001*
	No	45(38.1%)	26(22%)	47(39.8%)	
Vitamin-C	Yes	9(9%)	28(28%)	63(63%)	< 0.001*
	No	51(34.6%)	29(20.7%)	60(42.9%)	
Vitamin-E	Yes	8(8.3%)	25(26%)	63(65.6%)	< 0.001*
	No	52(36.1%)	32(22.2%)	60(41.7%)	
Corticosteroids	Yes	14(12%)	20(17.1%)	83(70.9%)	< 0.001*
	No	46(37.4%)	37(30.1%)	40(32.5%)	
KCl	Yes	4(5.5%)	6(8.2%)	63(86.3%)	< 0.001*
	No	56(33.6%)	51(30.5%)	60(35.9%)	
Magnesium sulfate	Yes	10(23.3%)	13(30.2%)	20(46.5%)	0.54
	No	50(25.4%)	44(22.3%)	103(52.3%)	
Gluconate calcium	Yes	11(22.4%)	12(24.5%)	26(53.1%)	0.89
	No	49(25.7%)	45(23.6%)	97(50.8%)	

Contd. table 2.

Bicarbonate	Yes	14(20.9%)	16(23.9%)	37(49.7 %)	0.63
	No	46(26.6%)	41(23.7%)	86(69.9%)	
Paraffin gavage	Yes	7(36.8%)	6(31.6%)	6(31.6%)	0.20
	No	53(24%)	51(23.1%)	117(52.9%)	
Norepinephrine	Yes	11(19%)	11(19%)	36(62%)	0.17
	No	49(26.9%)	46(25.3%)	87(47.8%)	
Antibiotic	Yes	2(2.7%)	5(6.8%)	67(90.5%)	< 0.001*
	No	58(34.9%)	52(31.3%)	56(33.7%)	
Ranitidine	Yes	4(7.7%)	17(32.7%)	31(59.6%)	< 0.001*
	No	56(29.8%)	40(21.3%)	92(48.9%)	
Pantoprazole	Yes	20(12%)	39(23.5%)	107(64.5%)	< 0.001*
	No	40(54.1%)	18(24.3%)	16(21.6%)	
Acetaminophen	Yes	0(0%)	4(7.8%)	47(92.2%)	< 0.001*
	No	60(31.7%)	53(28%)	76(40.2%)	
Diazepam	Yes	1(2.9%)	6(17.6%)	27(79.3%)	< 0.001*
	No	59(28.6%)	51(24.8%)	96(46.6%)	
Midazolam	Yes	5(5.2%)	18(18.8%)	73(76%)	< 0.001*
	No	55(38.2%)	39(27.1%)	50(34.7%)	
Dialysis	Yes	1(1.9%)	9(17%)	43(81.1%)	< 0.001*
	No	59(31.6%)	48(25.7%)	80(42.8%)	
ICU admission	Yes	4(3.4%)	22(18.5%)	93(78.2%)	< 0.001*
	No	56(46.3%)	35(28.9%)	30(24.8%)	
Intubation	Yes	13(12.3%)	18(17%)	75(70.7%)	< 0.001*
	No	47(35.1%)	39(29.1%)	48(35.8%)	
Clinical outcome	Recovery with no complications	47(27%)	41(23.6%)	86(49.4%)	0.50
	Recovery with neurological sequel	1(20%)	0(0%)	4(80%)	
	Death	12(19.7%)	16(26.2%)	33(54.1%)	

Results are expressed as numbers (percentages). Categorical variables were analyzed between groups using Fisher's exact test or Chi-square test. *According to the post hoc analysis, a significant difference was observed between group 3 (over 72 hours) and other groups.

frequently administered to the patients in the group that stayed more than 72 *hrs*. There was no significant association found between clinical outcomes and length of stay.

The statistical analysis revealed no significant differences between the groups for most laboratory findings. However, significant differences were observed in WBC count and magnesium levels among the three studied groups. Patients in the "over 72 *hrs*" group exhibited significantly higher WBC and lower magnesium levels.

Factors associated with LOS were examined using a multivariable linear regression model in table3. Benzodiazepines were found to reduce in LOS by 20 *min*, while antibiotic administration was associated to an increase in LOS by 20 *min*. Intensive care unit duration was also linked to an increase in LOS by 16 minutes. Furthermore, for every 1 *mg/dL* increase in

Table 3. Linear regression analysis of the factors associated with length of stay in patients with pesticide-induced thrombocytopenia

Variables		B(CI)	p-value
Insecticides	Insecticides	1	-
	Fungicides and herbicides	-0.12(-0.73-0.50)	0.70
	Rodenticides	-0.001(-0.617-0.615)	>0.99
	Others	-0.58(-1.24-0.08)	0.09
Poisoning severity	Mild	1	-
	Moderate	0.08(-0.16-0.32)	0.53
	Severe	0.17(-0.09-0.43)	0.20
Treatment protocols	Antidotes*	-0.06(-0.29-0.18)	0.65
	Antiapoptotic agents**	0.17(-0.13-0.48)	0.27
	Benzodiazepine***	-0.33(-0.56--0.10)	0.005
	Anti acid*****	0.17(-0.13-0.48)	0.27
	Acetaminophen	0.19(-0.010-0.40)	0.061
	Antibiotics	0.32(0.11-0.54)	0.003
	Dialysis	0.03(-0.29-0.34)	0.86
	Intensive care unit	0.27(0.08-0.46)	0.006
	Intubation	0.60(-0.83-(-0.36)	<0.001
Laboratory data	WBC count	0.001(-0.015-0.017)	0.91
	Magnesium level	-0.05(-0.09-(-0.01)	0.011

*Antidotes (pralidoxime, atropine), **Antiapoptotic agents (vitamin C, vitamin E, corticosteroids) and ***Benzodiazepine (diazepam, midazolam), ***** Antiacid (ranitidine, pantoprazole), Coefficients of linear regression (B), Confidence interval (CI).

blood magnesium levels, the length of stay decreased by 3 *min* ($p<0.05$).

Discussion

The current study investigated the impact of various factors on the LOS in patients with pesticide poisoning who developed thrombocytopenia either upon admission or during their hospitalization. Pesticide poisoning is an emerging health concern, especially in developing countries (23). Factors such as higher rates of agricultural activities, lower urban residency, and geographical and ecological differences may contribute to the increased incidence of pesticide intoxication in these regions (24). Pesticides can affect different tissues and systems, including hematological tissues and cells (25). Short-term exposure to pesticide has been shown to decrease monocytes, hemoglobin, and platelets, indicating a direct toxic effect on peripheral blood cells (26).

LOS, defined as the number of days a patient spends in the hospital after being admitted, is a critical measure for evaluating the cost-effectiveness of healthcare systems and reducing hospital-related complications (27). To the best of authors' knowledge, no previous studies have specifically examined the effects of various factors on LOS in this particular context.

The current study revealed that benzodiazepine administration was associated with reductions in LOS. However, antibiotic administration, ICU admission and intubation were significantly associated with longer length of stay.

This can be explained by the higher severity of poisoning requiring these interventions, which in turn contribute to extended hospital stays. The ICU is a structured system for treating seriously ill patients and logically influences LOS (28). Previous studies have shown that post-intubation complications, such as hypotension, can increase LOS (29), and

dialysis-related factors, such as elective surgeries and cardiovascular diseases, can also prolong the hospitalization (30,31). In parallel with the results, a previous study was shown that early, escalating therapy with benzodiazepines appears to decrease length of stay (32).

Moreover, the present study found a significant association between the type of pesticide toxicity and LOS, likely due to the higher need for ICU admission, additional monitoring, and clinical interventions. Herbicides and fungicides were associated with longer LOS, which could be attributed to their prolonged environmental persistence and the potential for more severe organ damage. These findings were in accordance with previous study results (33,34). Additionally, there was a significant association between paraquat concentration, as assessed by the dithionite test, and longer LOS, supporting the evidence of paraquat's toxic effects (35).

Another notable finding was the relationship between WBC count and LOS. This finding aligns with previous literature highlighting the correlation between elevated WBC counts and prolonged hospital stays (36-38). Platelet counts also indicated an association with LOS; higher platelet counts have been linked to extended hospitalizations in prior studies (39). Researchers have suggested that this may be due to increased disease severity or complications. Furthermore, Magnesium (*Mg*) concentration was significantly lower in patients with longer LOS. Hypomagnesemia is a well-known risk factor for prolonged hospitalization due to its impact on the immune system, respiratory function, cardiovascular health, and metabolic disturbances (40).

The effect of different drugs on LOS was evaluated, revealing that many medications could extend the length of stay. This is likely due to the higher usage rates of drugs such as diazepam and midazolam for sedation in intubated patients. The necessity of pralidoxime as an antidote for paraquats, which are among the various pesticides, also contributes to longer LOS. The increased administration of other drugs in more severe cases of intoxication further supports this finding.

Interestingly, there was no significant association between LOS and patient clinical outcomes. This lack of significance could be attributed to the impact of early deaths on the overall LOS, potentially obscuring the relationship between LOS and outcomes.

The study has several limitations. The small sample size and monocentric nature may introduce biases, and the retrospective design limits the study's conclusions. Additionally, post-discharge complications were not evaluated.

Conclusion

In conclusion, this study highlighted the impact of pesticide type and poisoning severity on LOS. Future multicentric studies with larger sample sizes are needed to better assess the predictive factors of LOS in these patients.

Acknowledgement

This research was approved by ethical approval obtained from the Ethics Committee under code IR.MUI.MED.REC.1400.381.

Conflict of Interest

There was no conflict of interest in this manuscript.

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