ORIGINAL ARTICLE

Clinicoepidemiological profile and outcome of patients with rat killer poisoning

Allwyn A[1], Yoganathan Chidambaram[1], Clement Jenil Dhas C P[1], Dilip Kumar[1], Navinkumar B K[1], Sujith kumar S[1]*

[1]Department of General Medicine, PSG Institute of Medical Sciences & Research, Peelamedu, Coimbatore-641004 (Tamil Nadu), India

Abstract

Background: Rodenticide poisoning is an important health problem with a high case fatality rate especially with metal phosphides. *Aim and Objectives:* To study and analyze the clinicoepidemiological features and outcomes of patients who have consumed different types of rat killer poison at a tertiary healthcare center located in Coimbatore, India. *Material and Methods:* The present retrospective observational study was conducted at a tertiary care hospital located in Coimbatore between January 2013 through December 2022. Patients above 16 years of age admitted with a diagnosis of rat killer poisoning were included in the study. Patients whose data was not available were excluded from the study. A sample size of 70 participants was considered and the study was conducted by assessing data retrieved from the medical records of the selected patients. *Results:* In the present study, the mean age of the participants was 27.13 ± 9.74 years, included an equal number of males and females, and 97.1% of participants had ingested the rodenticide deliberately with yellow phosphorus (50%) being the most ingested rodenticide. Most participants were discharged (68.6%), (8.6%) of the participants were deceased and (22.9%) had discharge against medical advice. Liver function tests showed that the mean direct bilirubin value, mean indirect bilirubin, mean Serum Glutamic Oxaloacetic Transaminase (SGOT) level, mean Serum Glutamic Pyruvic Transaminase (SGPT) level and International Normalized Ratio (INR) were all above the normal range. Regarding clinical manifestations, most participants suffered from vomiting (65.7%). The impact of medical interventions on clinical outcomes showed that gastric lavage (given within 2 hours) (p=0.008) and plasma therapy (p=0.001) significantly impacted the clinical outcome of the poisoning. *Conclusion:* The different clinical profiles assessed showed that rat killer poisoning can result in gastrointestinal symptoms and derangement in liver function tests. Plasma exchange therapy and gastric lavage were found to be effective treatment modalities in patient management.

Keywords: Epidemiology, Clinical Outcomes, Poisoning, Rodenticide

Introduction

Acute poisoning is the leading cause of morbidity and mortality across the globe with developing nations bearing 90% of the burden of poisoning deaths [1]. The global burden of rodenticide poisoning varies from region to region. In the United States, as per the American Association of Poison Control Centers, rodenticides accounted for 0.3% of 2.3 million human exposures as reported to the regional poison control centers [2]. In developed nations, the death rate from poisoning is 1-2%, while it ranges up to 20% in India. The nature of poisoning shows a regional variation depending upon the agent predominantly in use[1].

Deliberate Self-poisoning and Harm (DSPH) refers to an act of intentionally causing harm to oneself to

inflict bodily damage or consuming harmful compounds such as drugs or chemicals without suicidal intent. Triggers for such behavior include emotional stress/depression due to academic failure, family problems, workplace issues, romantic discord, or financial crises. Although these impulsive acts are performed without any suicidal intent, they can turn out to be very lethal depending on associated morbidity or mortality in worse cases [3]. These kinds of poisonings are compounded by the fact that fifty-seven million people (18% of the global estimate) in India are affected by depression [1].

Due to their widespread availability, rodenticide intake for attempting suicide is a serious issue in Asian nations. Most rodenticides are hepatotoxic in action and cause Acute Liver Failure (ALF) due to their varying chemical compositions and levels of toxicity. The toxicity of phosphorus-based rodenticide poisoning has been extensively documented in cases from all over the world, including North India, the United Kingdom, Australia, and Iran. It is also associated with a high mortality rate. According to a recent study from South India, yellow phosphorus was the most popular rodenticide used in suicide attempts there, with a 30% fatality rate despite maximal supportive therapy [4]. RATOL is a popular brand of yellow phosphorous freely available in India. It is available as pastes containing 2–5% of yellow phosphorous. Yellow phosphorous poisoning is common in children as the paste is mistaken for toothpaste, or bread smeared with this paste as bait could be accidentally consumed [5]. Brodifacoum is another rodenticide component belonging to a group commonly referred to as "superwarfarins" or "Long- Acting" Anticoagulant Rodenticides (LAARs) which is 100 times more potent than warfarin with respect to anticoagulant effects [6].

Rodenticide poisoning is an important health problem with a high case fatality rate especially with metal phosphides. These are also made easily available by means of over-the-counter sales or e-commerce websites. A lack of antidotes for rodenticides in our country results in this type of poisoning becoming an important health problem. Improving public awareness regarding their lethality and strict monitoring of sales and usage of rodenticides could help to avoid indiscriminate use and poisoning. It is important to know the various clinical presentations and complications which are very diverse based on the chemical compound associated with the poison. Toward this end, the present study was conducted with the aim of assessing the clinicoepidemiological features and outcomes of patients with rat killer poisoning.

Material and Methods

The present retrospective observational study was conducted at a tertiary care hospital located in Coimbatore between January 2013 through December 2022. The study was initiated after obtaining clearance from the Institutional Human Ethics Committee (IHEC) with reference number PSG/IHEC/2023/Appr/Exp/107 and patients were selected after obtaining necessary informed consent. All patients admitted to the hospital during the study period were included in the study.

Sample size estimation

The sample size was estimated based on the results of a previously conducted study [7]. The chi-square test was conducted with an effect size of 0.4 and a significance level of 0.05. The desired statistical power was set at 0.80, indicating an

80% probability of detecting a true effect if it exists. The degrees of freedom were calculated based on the number of categories in the variable of interest. The resulting sample size N required to achieve the specified power was approximately 68.14. This indicates that, to detect the specified effect size with a power of 0.80 and a significance level of 0.05, a sample size of approximately 68 observations would be needed. A sample size of 70 was considered for the present study.

Methodology

Patients above 16 years of age admitted with a diagnosis of rat killer poisoning were included in the study. Patients whose data were not available were excluded from the study along with patients who had ingested mixed poisons or suffered from chronic liver disease. Eight-two patients were selected for the study and this number was reduced to 70 based on the inclusion and exclusion criteria and these cases were followed up. The demographic details of the participants were collected along with clinical manifestations and outcomes. Liver function tests like direct bilirubin, indirect bilirubin, Serum Glutamic Oxaloacetic Transaminase (SGOT), Serum Glutamic Pyruvic Transaminase (SGPT), and International Normalized Ratio (INR) were performed. Renal function tests were recorded by assessing creatinine, bicarbonate, sodium, calcium, potassium, and serum lactate levels. The participants were treated by means of gastric lavage (given within 2 hours), plasma exchange and/or N-acetylcysteine (NAC) treatment. Clinical outcome was described based on the following: Discharge Against Medical Advice (DAMA), deceased, no follow-up, and recovered. All patients who were discharged against medical advice were later in moribund state. The collected information was entered into data sheets for statistical analysis.

Statistical analysis

Analysis was done using SPSS v 24.0. Descriptive statistics were performed, and results were shown in frequency and percentage. Test for association was performed using the Chi-square test, Kruskal-Wallis test and Mann-Whitney U test, value of $p < 0.05$ was considered statistically significant.

Results

Demographic details (Table 1)

In the present study, the demographic data showed that the mean age of the participants was 27.13 ± 9.74 years, and gender distribution showed an equal number of males and females. Most of the participants belonged to rural areas (75.7%) and 97.1% participants had ingested the rodenticide deliberately. Most participants did not report any prior psychiatric illness (87.1%). Most participants had consumed the rodenticide in the form of paste (50%) followed by cake (40%) and in most participants, the amount of rodenticide consumed was 25 g (28.6%) followed by 30 g (21.4%). When assessing the compound in rodenticide, yellow phosphorus (50%) was the most common followed by bromadiolone 0.005 (40%).

Presentation of outcomes and clinical manifestations among participants (Table 2)

Most participants were discharged (68.6%) while 8.6% participants were deceased and 22.9% participants had taken DAMA. During follow-up, 60% participants were found to have recovered.

Table 1: Demographic details of participants

Parameters		Count (N)	Percentage (%)
Gender	**Female**	35	50.0
	Male	35	50.0
Rural	**No**	17	24.3
	Yes	53	75.7
Deliberate	**Accidental**	2	2.9
	Yes	68	97.1
Prior Psychiatric Illness	**No**	61	87.1
	Yes	9	12.9
Consumption Type	**Cake**	28	40.0
	Paste	35	50.0
	Powder	7	10.0
Consumption Quantity (grams)	**5**	5	7.1
	10	14	20.0
	15	10	14.3
	20	3	4.3
	25	20	28.6
	30	15	21.4
	50	3	4.3
Compound In Rodenticide	**Bromadiolone 0.005%**	28	40.0
	Yellow Phosphorus	35	50.0
	Zinc Phosphide	7	10.0

Table 2: Outcome analysis of participants

Parameters		Count (N)	Percentage (%)
Discharged		48	68.6
Deceased		6	8.6
DAMA*		16	22.8
Total		70	100
Follow Up	**NA**	22	31.43
	No follow up	6	8.57
	Recovered	42	60
	Total	70	100

**DAMA- Discharge Against Medical Advice*

Impact of laboratory parameters on clinical outcomes (Table 3)

The Kruskal-Wallis test revealed a statistically significant difference in direct bilirubin levels among the three outcomes (DAMA, deceased, discharged) with *p* value of 0.000. A highly significant difference was observed in SGOT, SGPT, INR, bicarbonate, ionized calcium, and serum lactate levels among the outcomes (p = 0.000). Potassium levels also showed a significant difference (p = 0.001) among the clinical outcomes among the study participants.

Clinical presentations based on type of rodenticide poisoning (Table 4)

Presence of abdominal pain significantly varied among individuals exposed to different rodenticides (p=0.000). Specifically, a statistically significant difference was observed in the presence of abdominal pain among those exposed to bromadiolone 0.005%, yellow phosphorus, and zinc phosphide. A similar result was seen with respect to vomiting (p = 0.000) indicating that the type of rodenticide had an impact on the likelihood of experiencing vomiting. The presence of jaundice also showed a significant association with the type of rodenticide (p = 0.000). There was a significant difference in the presence of bleeding tendencies based on the type of rodenticide exposure (p = 0.043). For other clinical symptoms (lethargy, restlessness, altered mental status, seizures, palpitation, and breathing difficulty), no significant associations were found with the type of rodenticide exposure.

Association between clinical outcomes and gender, consumption quantity, compound type and different medical interventions in rodenticide poisoning cases (Tables 5 & 6)

When the association between clinical outcomes and select variables was analyzed, it was found that

the distribution of outcomes (DAMA, deceased, no follow-up, and recovered) did not significantly differ between genders and the amount of rodenticide consumed. However, a statistically significant association was found between clinical outcomes and compound in rodenticide ($p = 0.041$).

On assessing the impact of medical interventions on clinical outcomes, it was found that gastric lavage (given within 2 hours) ($p = 0.008$) and plasma therapy ($p = 0.001$) significantly impacted the clinical outcome of the poisoning. N-acetylcysteine (NAC) treatment did not show a significant association with the clinical outcomes ($p=0.092$).

Table 3: Impact of laboratory parameters on clinical outcomes

Parameters	Outcome			Kruskal Wallis Test Statistic	*p*
	DAMA	Deceased	Discharged		
	Mean ± SD	Mean ± SD	Mean ± SD		
Direct bilirubin	3.4 ± 2.9	4.3 ± 2.5	1.0 ± 1.6	15.252	**0.000***
Indirect bilirubin	1.7 ± 1.6	1.7 ± 2.6	1.1 ± 1.6	3.229	0.199
SGOT[#]	1884 ± 2751	3565 ± 3818	238 ± 450	17.374	**0.000***
SGPT**	695 ± 656	1091 ± 686	167 ± 286	16.359	**0.000***
INR[##]	6.45 ± 6.36	7.33 ± 5.99	1.56 ± 0.86	18.054	**0.000***
Creatinine	0.85 ± 0.52	1.73 ± 1.04	0.75 ± 0.24	5.104	0.078
Bicarbonate	19.3 ± 3.8	5.3 ± 4.4	22.3 ± 2.1	22.138	**0.000***
Sodium	136 ± 7	136 ± 5	138 ± 4	1.755	0.416
Ionized calcium	0.921 ± 0.200	0.908 ± 0.086	1.106 ± 0.108	19.654	**0.000***
Potassium	3.20 ± 0.51	2.96 ± 0.33	3.60 ± 0.44	13.113	**0.001***
Serum lactate	7.14 ± 5.43	16.94 ± 9.68	2.15 ± 2.44	19.925	**0.000***

*[#]SGOT: Serum Glutamic Oxaloacetic Transaminase; **SGPT: Serum Glutamic Pyruvic Transaminase;*
[##]INR: International Normalized Ratio

Table 4: Differential clinical symptomatology in rodenticide poisoning: Impact of rodenticide type

Parameters		Compound In Rodenticide			Test Statistic	*p*
		Bromadiolone 0.005%	Yellow Phosphorus	Zinc Phosphide		
Abdominal pain	**No**	23	11	4	16.147	**0.000***
	Yes	5	24	3		
Vomiting	**No**	16	4	4	16.232	**0.000***
	Yes	12	31	3		
Lethargy	**No**	24	33	5	3.387	0.184
	Yes	4	2	2		
Restlessness	**No**	27	32	7	1.193	0.551
	Yes	1	3	0		
Altered mental status	**No**	28	30	7	5.835	0.068
	Yes	0	5	0		
Seizures	**No**	28	34	7	1.014	0.602
	Yes	0	1	0		
Palpitation	**No**	27	34	7	0.257	0.879
	Yes	1	1	0		
Breathing difficulty	**No**	28	32	7	3.134	0.209
	Yes	0	3	0		
Jaundice	**No**	28	19	6	18.102	**0.000***
	Yes	0	16	1		
Bleeding tendencies	**No**	27	27	7	6.311	**0.043***
	Yes	1	8	0		

**-Statistically significant ($p<0.05$)*

Table 5: Association between clinical outcomes and gender, consumption quantity, compound type and different medical interventions in rodenticide poisoning cases

Parameters		Result				Test Statistic	*p*
		DAMA	Deceased	No follow up	Recovered		
Gender	**Female**	10	3	1	21	4.596	0.204
	Male	6	3	6	20		
Consumption Quantity (grams)	**5**	2	0	1	2	22.795	0.199
	10	2	1	2	9		
	15	5	0	0	5		
	20	1	0	0	2		
	25	1	1	3	15		
	30	5	3	0	7		
	50	0	1	1	1		
Compound in Rodenticide	**Bromadiolone 0.005%**	4	0	5	19	13.10	**0.041***
	Yellow Phosphorus	11	6	1	17		
	Zinc Phosphide	1	0	1	5		
Gastric lavage given < 2 hour	**No**	11	5	0	20	11.894	**0.008***
	Yes	5	1	7	21		
NAC	**No**	1	0	3	11	6.445	0.092
	Yes	15	6	4	30		
Plasma	**No**	11	1	7	36	18.558	**0.001***
	Yes	5	5	0	5		

**-Statistically significant ($p<0.05$)*

Discussion

The prevalence of stress and depression among all kinds of population has been studied extensively with depression affecting about 350 million people. Excessive level of stress and depression can lead an individual to take grievous action like suicide to escape the reality of their problems [8-9]. Rodenticides include diverse component substances ranging from yellow phosphorous to super warfarins.

Among these, yellow phosphorus ranks highly in the mortality hierarchy because it has been shown to result in fulminant hepatic failure and hepatocellular necrosis [7]. Because Low Middle Income Countries (LMIC), especially in the Asia-Pacific region are economies based mainly on agriculture, the availability of rodenticides is high which can result in the incidence of poisoning [10-11].

In the present study, the mean age of the participants was 27.13 ± 9.74 years, and gender distribution showed an equal number of males and females. Most of the participants (97.1%) had ingested the rodenticide deliberately and most participants belonged to rural areas (75.7%). These results are similar to those obtained in a study conducted by Radhakrishnan *et al*., where the majority of patients who had ingested rodenticide belonged to the age group of 18-30 years (43.75%) but had a higher number of male participants (68.75%) [12]. Another study by Das *et al*., also reported that most participants were aged between 21-30 years (42%), had gender distribution close to 50% and most participants had ingested rodenticide deliberately (98%) [13]. The history of ingestion was similar to the results of a study conducted by Yan *et al*. wherein of the 31 participants with a history of ingestion, 30 patients had ingested rodenticide deliberately as a suicide attempt [14]. With regard to locality, a previously conducted study by Tassew *et al*. reported a similar majority of participants aged between 20-40 years, 53.21% were females and most participants belonged to rural areas (83.97%) [15].

Most participants had consumed the rodenticide in the form of paste (50%) followed by cake form. This was similar to another study which found that the majority of participants ingested rodenticide in paste form (72%) [16]. When assessing the compound in rodenticide, yellow phosphorus (50%) was the most common followed by bromadiolone 0.005% (40%). This result contrasted with that of a previously conducted study wherein the most common type of rodenticide consumed were super warfarins (87.8%) which include bromadiolone [14]. However, A previously conducted study had also reported that yellow phosphorus was the most common rodenticide that was encountered by emergency departments [15].

When the outcomes were enumerated, most participants were found to have been discharged (68.6%) and 8.6% of the participants were deceased. Regarding discharge AMA, 22.8% of participants had left the hospital that way. During follow-up, 58.6% of participants were found to have recovered. The results are in contrast with the results of a study conducted by Mohanka *et al*. in which only about 18% of participants had discharged themselves AMA which is lower than the present study [17]. Another study conducted by Govindarajan *et al*. reported that among participants who had ingested rodenticide, 64% had been discharged post treatment which was close to the result of the present study, 29% had passed away which was much higher than the present results and 6% had been discharged AMA which is a very low number compared to the present study [16]. This difference in results can be attributed to the vast difference in sample size between studies (70 vs. 450).

Regarding clinical manifestations, most participants suffered from vomiting (65.7%) followed by abdominal pain and jaundice. The presence of abdominal pain, vomiting, jaundice, and bleeding tendencies significantly varied among individuals

exposed to different rodenticides ($p = 0.000$). The results of a previously conducted study reported that the most common symptoms were nausea and vomiting followed by abdominal pain and jaundiced eyes which were in line with the results of the present study [12]. Another study reported that 84.2% of participants had presented with jaundice at admission which is in contrast with the present results [16-17]. Previous studies have reported that rodenticides cause gastrointestinal symptoms initially which further progress to systemic multi-organ failure, prominently cardiotoxicity, and ALF which are often fatal [15, 18-19]. Recent literature has also reported the presence of subarachnoid hemorrhage in patients suffering from bromadiolone poisoning [20].

The results revealed a statistically significant difference in the direct bilirubin, SGOT, SGPT, INR, bicarbonate, ionized calcium, and serum lactate levels among the patients based on the three outcomes (AMA, deceased, discharged). Elevated levels of direct bilirubin may be associated with distinct clinical trajectories, potentially serving as a prognostic marker. A highly significant difference was observed in SGOT, SGPT INR and bicarbonate levels among the outcomes. SGOT, SGPT, INR and bicarbonate levels may play a significant role in differentiating clinical trajectories, suggesting its relevance as a prognostic indicator. This difference can be explained by the values being well above the normal range in the deceased and AMA group when compared to the discharge group hinting at liver damage due to ingestion of rodenticide. Another previously conducted study also reported a significant association between rodenticide poisoning and a higher rate of INR rebound after administration of an antidote ($p < 0.05$) which confirms it's direct action on the lethality of rodenticide [14].

When the association between clinical outcomes and select variables was tested, a statistically significant association was found between clinical outcomes and compounds in rodenticide ($p = 0.041$). This can be explained by the differing levels of lethality between the three rodenticide components. The impact of medical interventions on clinical outcomes was assessed showing that gastric lavage ($p = 0.008$) and plasma therapy ($p = 0.001$) significantly impacted the clinical outcome of the poisoning while NAC treatment did not show an association. A previously conducted study also reported that Therapeutic Plasma Exchange (TPE) treatment showed a statistically significant ($p < 0.05$) improvement in liver function which is similar to the results of the present study [12]. Conversely, a few studies reported that NAC treatment had been useful in the management of rodenticide poisoning [21-23].

The study was not without limitations. The sample size of the study was less, and the single-centered nature of the study did not add to the generalizability of the study. The clinical implications of the study are that the results reinforce the need for quick response and treatment of the patients to ensure better chances of recovery and lower mortality. This can be achieved by educating healthcare professionals on the different clinical symptoms described in the present study to diagnose deliberate and occult rodenticide poisoning to provide faster treatment. The study has also pointed out to the adverse effect poisoning has on the renal function which has not been studied extensively. These results of the present study would benefit from further research by

including a larger sample size and multiple health centers.

Conclusion

The results of the present study help conclude that education on the clinical profile, complications, and outcome of patients with rodenticide poisoning might help us to treat patients more efficiently thereby reducing mortality. This can also help in planning public awareness programs at a community level for prevention.

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Author for Correspondence:
Dr. Yoganathan Chidambaram, Department of General Medicine, PSG IMS & R, Peelamedu, Coimbatore-641004, Tamil Nadu, India
Email: yoganathancc@gmail.com Cell: 9942460735

How to cite this article:
Allwyn A, Chidambaram Y, Clement JDCP, Kumar D, Navinkumar BK, Kumar SS. Clinicoepidemiological profile and outcome of patients with rat killer poisoning. *J Krishna Inst Med Sci Univ* 2023; 12(4):99-110

Submitted: *01-July-2023* ***Accepted:*** *01-Sep-2023* ***Published:*** *01-Oct-2023*