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Benzodiazepines: Predominant Reported Acute Poisoning to Private Sector Tertiary Care Hospitals in Karachi

Qudsia Hassan[1], Muhammad Ikram Ali[1], Azra Anwar[2], Syed Hasan Danish[3], Abdullah Ashraf[4]

[1]Forensic Medicine & Toxicology Department, Ziauddin University, [2]Jinnah Medical & Dental College, Jinnah Hospital, Lahore, [3]Community Health Sciences Department, Ziauddin University, [4]Jinnah Hospital, Lahore.

ABSTRACT

Background: Acute poisoning is a major medical emergency that translates into morbidity and mortality across all age groups, it is a potentially preventable cause of illness and death. This study was carried out to assess the epidemiological information of acute poisoning among the general population presented to the three campuses of a private tertiary care teaching hospital in Karachi, Pakistan.

Methods: The cross-sectional study was conducted at three campuses of a private tertiary care teaching hospital, Dr. Ziauddin Hospital in Karachi, comprising of records from January 1, 2018, to December 31, 2022, of patients reporting acute poisoning. These records were accessed after getting approval from the Ethical review committee. Consecutive sampling technique was applied while data was collected. All cases of acute poisoning reporting to the emergency department with complete records were included. While data of those with any other diagnosis or incomplete record were excluded. Descriptive analysis was performed for quantitative variables. For categorical data frequency and percentages were extracted. The chi-square test was used to associate categorical variables. P value less than 0.05 was taken as statistically significant.

Results: : The total number of cases was n=518 out of which n=235 (45.4%) were males while n=283 (54.6%) were females and the maximum number of cases n=111 (21.4%) were associated with Benzodiazepines followed by insecticide poisoning and ingestion of rodenticides.

Conclusion: The most susceptible groups to acute poisoning were found to be women and children. A prevalent agent that caused toxicity was benzodiazepines; the biggest number of cases occurred in April, while the lowest number occurred in December. The year 2020 was linked to the highest number of cases.

Keywords: Poisoning, Toxicology, Benzodiazepines, Insecticides, Forensic Toxicology.

Corresponding Author:
Dr. Muhammad Ikram Ali
Associate Professor,
Dept. Forensic Medicine & Toxicology,
Ziauddin University.
Email: ikram.ali@zu.edu.pk
Office Address: 4/B, Shahrah-e-Ghalib, Clifton, Block 6, Karachi.
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INTRODUCTION

Paracelsus the herald of modern toxicology believed everything is a poison and it's the dosage that holds a pivotal role [1]. A poison is any substance that is associated with harmful effects on the human body when ingested, injected, inhaled, or absorbed via the skin. Poisoning can be intentional or accidental [2]. Even normally nonpoisonous substances, when taken in excess have the potential to cause poisoning [3].

Acute poisoning is a major medical emergency that translates into morbidity and mortality across all age groups [4,5]. Poisoning, globally results in an annual loss of 7.4 million healthy lives, as per the World Health Organization (WHO) statistics. Acute poisoning cases are the second largest cause of morbidity after road traffic accidents (RTAs) [6]. Acute poisoning is also one of the most common causes of visits to the emergency department and hospitalizations [7]. According to WHO majority of the cases of poisoning are reported from low-income and middle-income countries, similarly, the mortality rates as a result of acute poisoning are higher in developing countries as compared to the more developed economies [8]. The incidence of poisoning is increasing due to rapid lifestyle modifications and social behavioral changes [1].

Acute poisoning is a potentially preventable cause of illness and death, it is important to study the epidemiological variations of acute poisoning in different populations across the globe along with the identification of causative substances associated with this serious health concern[9].

This study was carried out to assess the epidemiological information of acute poisoning among the general population presented to the three campuses of a private tertiary care teaching hospital in Karachi, Pakistan.

METHODS

The cross-sectional, study was conducted at three campuses of a private tertiary care teaching hospital, Dr. Ziauddin Hospital, in Karachi, located in North Nazimabad, Clifton, and Kemari, comprising of records from January 1, 2018, to December 31, 2022, of patients reporting with acute poisoning. These records were accessed after getting approval from the Ethical review committee and all the records were anonymized at the time of data collection, A consecutive sampling technique was applied while data was collected.

Records of all the patients presenting to the Emergency department of the three campuses of a private tertiary care teaching Hospital, in Karachi, with the diagnosis of acute poisoning were included, while data of those with any other diagnosis or those with incomplete records were excluded. The diagnosis was based on presenting complaints, history, clinical picture, and laboratory findings. After anonymizing the data, relevant details like age, gender, the causative agent of poisoning, month and date of reporting, and outcomes were recorded. Based on a proportion of 50%, keeping precision at 5% the total sample was n=384. By adding 20% wastage our sample size was n=450. However, we included all records hence our sample was n=518.
Similarly concerning age, data was divided into four groups; children aged 1-10 years, adolescents aged 11-19 years, adults aged 20-59 years, and elderly aged 60 years or more.

Data was analyzed using SPSS version 27. Descriptive analysis was performed for numerical data by using mean and standard deviation, while categorical data was expressed as frequencies and percentages. Associations between categorical data were assessed using the chi-square test. P value less than 0.05 was taken as significant.

RESULTS

The total number of cases reported to the three campuses of a private sector tertiary care hospital was n=518 from 1st January 2018 to 31st December 2022 out of which n=235 (45.4%) were males while n=283 (54.6%) were females, the maximum number of cases n= 111 (21.4%) were associated with Benzodiazepines followed by insecticide poisoning and ingestion of rodenticides, besides this it is also notable that in n=131 (25.3%) of cases the cause of poisoning remained unknown. The frequency and percentages of the poisonous substances with the number of reported cases are presented in (Table 1).

Table 1: The Frequency and Percentages of Poisonous Substances with The Number of Reported Cases.

Toxic Substance	Number of Cases	Percentage
Benzodiazepines	111	21.4
Insecticides	95	18.3

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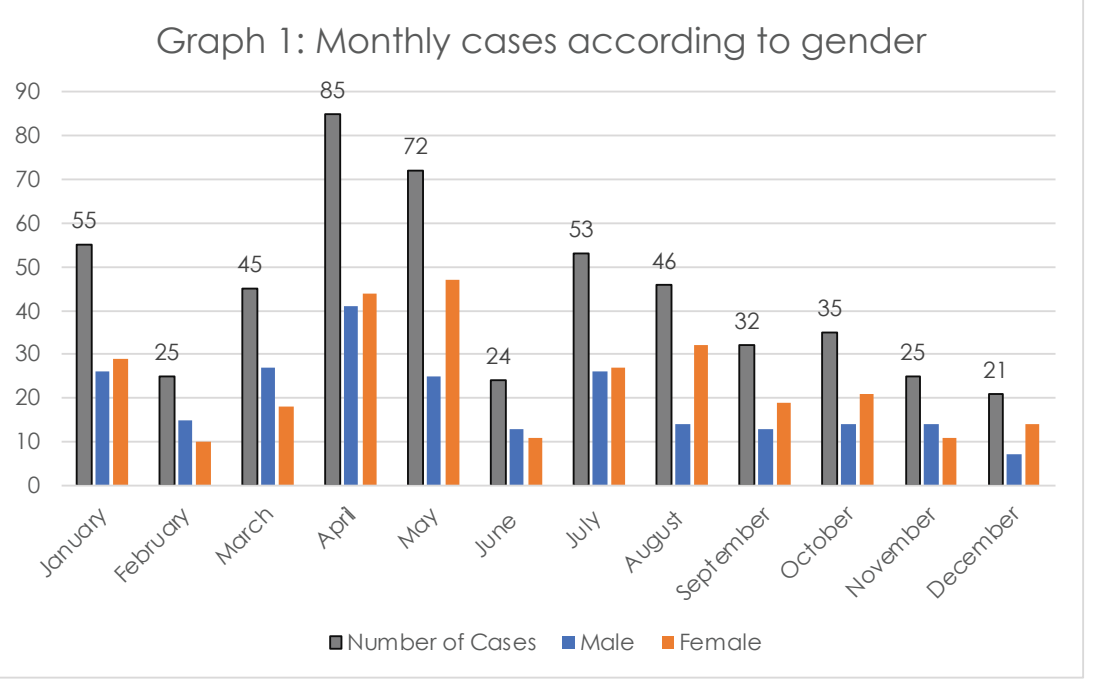
Rodenticide	82	15.8
Paracetamol	32	6.2
Antiepileptics	22	4.2
Alcohol	16	3.1
Kala pathar, (Paraphenylenediamine-PPD)	15	2.9
Snakebite	9	1.7
Cannabis	5	1
Unknown	131	25.3

With respect to the age of the victims it was noted that most patients were categorized as children, n=319 (61.6%) followed by patients that belonged to the adolescent age group, n=154 (29.7%), and n=36 (6.9%) in the middle-aged category and the least number of patients, n=9 (1.7%) were categorized as being elderly.

Annual distribution of these patients showed that the greatest number of cases was seen in the year 2020, n=148 (28.5%) followed by the year 2022, n=140 (27.0%) while the least number of cases, n=49 (9.4%) was seen in the year 2019, similarly n=66 (12.7%) was seen in the year 2018 and n=115 (22.2%) cases were observed in the year 2021. When the cases were analyzed according to the months it was noticeable that the highest number of cases were reported in April n=85 (16.4%) followed by May, n=72 (13.9%) while the minimum number of cases were seen in December n=21 (4.1%) followed by June n=24 (4.6%) and November n=25 (4.8%) a detailed distribution of reported cases in months along with gender-based differentiation is shown in Graph 1.



Graph 1: Showing Distribution of Reported Cases in Months Along with Gender-Based Differentiation

Regarding outcomes it was noted that n=41 (8.5%) patients expired, referrals were given to the OPD in cases of n=22 (4.2%) patients, while n=14(2.7%) patients were referred to the psychiatric department. In most of the cases, n=377 (72.8%) patients were discharged after appropriate treatment, and another n=61 (11.8%) patients left against medical advice (LAMA). It is worth mentioning that the highest mortality was seen in association with benzodiazepines as n=11 (9.9%) patients expired, while recovery in cases of Black stone poisoning was much better as no life was lost, a detailed comparison of poisonous substances and outcomes using chi-square test is shown in (Table 2).

Table 2: Comparison of Poisonous Substances and Patient Outcomes Using Chi-Square Test.

Toxic Substance	Outcome										P- value
	Expired		Discharged (After treatment)		OPD (Referral)		Psychiatry (Referral)		LAMA		
	n	%	n	%	n	%	n	%	n	%	
Benzodiazepines	11	9.9	78	70.3	6	5.4	1	0.9	15	13.5	0.564
Insecticides	10	10.5	70	73.7	4	4.2	2	2.1	9	9.5	0.869
Rodenticide	5	6.1	62	75.6	3	3.7	2	2.4	10	12.2	0.927
Paracetamol	3	9.4	23	71.9	2	6.2	3	9.4	1	3.1	0.086
Antiepileptics	2	9.1	15	68.2	0	0	0	0	5	22.7	0.404
Alcohol	1	6.2	11	68.8	0	0	0	0	4	25	0.443
Kala pathar, (Paraphenylenediamine-PPD)	0	0	12	80	1	6.7	1	6.7	1	6.7	0.579
Snakebite	1	11.1	5	55.6	1	11.1	0	0	2	22.2	0.634
Cannabis	1	20	2	40	0	0	0	0	2	40	0.258
Unknown	10	7.6	99	75.6	5	3.8	5	3.8	12	9.2	0.691

Comparisons of poisonous substances with different ages revealed that the incidence of acute toxicity by benzodiazepines was highest in children and adolescent age categories n=67 (60.4%) and n=37(33.3%) while in adults aged 20-59 years insecticide poisoning was highest n=9 (9.5%) a detailed comparison with chi-square test is shown in (Table 3).

Table 3: Comparison of Poisonous Substances and Patient Age Categories, Using Chi-Square test

Toxic Substance	Children (1-10 years)		Adolescents (11-19 years)		Adults (20-59 years)		elderly (60 years or more)		P-value
	n	%	n	%	n	%	n	%	
Benzodiazepines	67	60.4	37	33.3	06	5.4	01	0.9	0.636
Insecticides	61	64.2	23	24.2	09	9.5	02	2.1	0.479
Rodenticide	53	64.6	21	25.6	04	4.9	04	4.9	0.077
Paracetamol	17	53.1	14	43.8	01	3.1	00	00	0.266
Antiepileptics	14	63.6	08	36.4	00	00	00	00	0.503
Alcohol	12	75	4	25	00	00	00	00	0.564
Kala pathar, (Paraphenylene diamine-PPD)	09	60	03	20	03	20	00	00	0.208
Snakebite	06	66.7	03	33.3	00	00	00	00	0.832
Cannabis	03	60	02	40	00	00	00	00	0.892
Unknown	77	58.8	39	29.8	13	9.9	02	1.5	0.475

A comparison between age and gender showed that there were more cases of acute poisoning in males belonging to the younger age group n=155 (66%) and the least cases were reported in the elderly age group n=5 (2.1%), similarly, there were a female predominance in the adolescent n=94(33.2%) and middle age group n=21(7.4%). When patient's age categories were compared to the outcome it was revealed that the highest rate of mortality was n=27(8.5%) deaths seen in the youngest age group till 10 years of age, and similarly post-treatment recovery rate was also n=241(75.5%) in the youngest age group while there were no deaths noted in the elderly population having age 60 years or more. The detailed comparison of patient age categories with outcomes is shown in (Table 4).

Table 4: Comparison Between Patient's Age Outcome

Patient Age	Outcome									
	Expired		Discharged (After treatment)		OPD (Referral)		Psychiatry (Referral)		LAMA	
	n	%	n	%	n	%	n	%	n	%
Children (1-10 years)	27	8.5	241	75.5	12	3.8	04	1.3	35	11.0
Adolescents (11-19 years)	15	9.7	104	67.5	09	5.8	08	5.2	18	11.7
Adults (20-59 years)	02	5.6	24	66.7	01	2.8	01	2.8	08	22.2
elderly (60 years or more)	00	00	08	88.9	00	00	01	11.1	00	00
P-value: 0.134										

DISCUSSION

The highest number of cases reported with acute poisoning was in the year 2020 while overall the number of cases being reported to the hospital showed a steady increase in the rest of the years excluding the year 2021 in which the number of cases was above all the previous year excluding 2020. It can be declared keeping in view these statistics that the number of cases is increasing annually however there was a spike noted in the cases in the year 2020. The high incidence of cases in the year 2020 as compared to 2021 was also

observed according to certain American statistics as was declared in the 39th Annual Report of America's Poison Centers' National Poison Data System (NPDS)[10]. This can be an important finding which may be associated with increased suicidal tendencies being observed in the general population as globally the world was facing COVID-19 related restrictions and social isolation, during this period the burden of suicide also increased because of economic and social effects along with fear of COVID-19, in contrast to this finding another five-year study done within Karachi, at the National Poison Control Center showed a related decline in the number of reported cases in the year 2020[11-13]. The male is to female ratio according to our research is 0.83: 1, with females being more affected as compared to males this finding is more in contrast with a study done in the eastern part of India[14]. Another similar study done in Multan; a city in Pakistan showed a female predominance as was noted in our study[15]. The female predominance can be associated with an increased tendency of deliberate self-harm and attempted suicide associated with the female sex; another aspect of this finding is related to the culturally male dominant society that exists in Pakistan resulting in increased social pressures for the females in general[16,17].

In our study, most reported cases were those of children and the highest mortality was also seen in the same age group this finding is in contrast to most of the studies done in India and Pakistan that have identified the more productive age group 20 to 30 years as being the most vulnerable age for acute poisoning [3,18]. It's a possibility that these researches may not have included the younger age group as most of those cases could have been referred to pediatric emergencies, secondly, the tendency of accidental poisoning is higher in the younger age group a fact that has been expressed previously by stating that the cases of acute poisoning decline as the age increases [18,19]. Another important observation that has been associated with this fact is also reinforced in our research that most of the medicines are responsible for cases of poisoning in the younger age group being ingested accidentally by children[20]. Most of the cases in our research have been attributed to Benzodiazepines. The finding in our research in the aspect that a maximum number of cases are attributed to Benzodiazepines is also in contrast to most recent studies reported from the National Poison Control Center in Karachi[3,13]. Most of the cases were associated with insecticides in those studies which is the second highest reported attributable cause of mortality in our study.

There was no new poisonous agent identified in this study all the agents discussed have been documented in the previous studies done in Karachi [3,13]. An important aspect related to poisonous substances was that most deaths resulted from PPD or Kalapathar poisoning in most research done in Pakistan and India, where a legal ban has not been imposed on the trade of this particular substance[21,22,13]. This finding is in contrast to our research as a comparatively greater number of deceased were suffering from benzodiazepine poisoning followed by insecticides and rodenticides, this is a matter that can be attributed to the fact that PPD is a difficult-to-treat substance that is mostly ingested with suicidal intent and those cases need to be reported to the medicolegal section for any legal persecution later on, as suicide was considered a punishable crime according to Pakistani Law till December 2022 when its status as a punishable offense was denounced[23,24]. These cases would have been under-reported in our study setting as the study sites were tertiary care private hospitals lacking the legal framework.

The strengths of this study comprise five years that were included as the study period and the inclusion of three facilities located in three different regions of Karachi, a densely populated urban city [25]. As the data of a private sector hospital was utilized it represents most of the cases associated with accidental poisoning rather than deliberate self-harm or suicidal attempts as mostly those cases are reported to the public center hospitals where a medicolegal entry of the case is taken into consideration. However, that does not mean that deliberate self-harm and suicidal attempts are not reported to the private sector hospitals in Pakistan and the fact that even such cases are reported in the disguise of accidental poisoning to hide the commission of a recognized offense presents a challenge to such studies. The study could have been improved by including data from other public and private sector hospitals to get a more accurate analysis and a better picture of acute poisonings in the densely populated city of Karachi.

CONCLUSION

Females and children were identified as being most vulnerable to acute poisoning. The most common agent causing toxicity was benzodiazepines, the number of cases were highest in April to while lowest number of cases were seen in December, the year 2020 was associated with the highest number of cases.

CONFLICT OF INTEREST

None to declare

ETHICAL APPROVAL

The study was provided waiver by the Ethical Review Committee of Ziauddin University Reference # 4190821MIFOR.

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AUTHORS CONTRIBUTIONS

QH, Conceptualized and supervised; **MIA**: Conceptualized and wrote the article; **AA:** Collected data and designed the methodology; **SHD**: performed data analysis and also aided in the critical review; **AA**: Performed data analysis and helped in result writing.

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