



Risk Factors and Outcome of Acute Poisoning in Childrens

Abdul Sami Qureshi^{1*}, Farhana Zafar², Madiha Waseem³, Muhammad Taimor⁴ and Sobia⁴

¹Department of Emergency Medicine, Ziauddin University Hospital Karachi, Pakistan.

²Pediatrics, Ziauddin University Hospital Karachi, Pakistan.

³Department of Pediatrics, Ziauddin University Hospital Karachi, Pakistan.

⁴Department of General Surgery, Ziauddin University Hospital Karachi, Pakistan.

Authors' contributions

This work was carried out in collaboration among all authors. Author ASQ designed the study, wrote the protocol and wrote the first draft of the manuscript. Author FZ read and approved the final manuscript. Author MW managed the literature searches. Author MT managed the analyses of the study. Author S performed the statistical analysis. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/AJMAH/2021/v19i630336

Editor(s):

(1) Dr. Janvier Gasana, Kuwait University, Kuwait.

Reviewers:

(1) Melaku Getachew, Haramaya University, Ethiopia.

(2) G. Ulufer Sivrikaya, R. M. K Academy of Interventional Medicine, Education and Simulation (RMK AIMES), Turkey.

Complete Peer review History: <http://www.sdiarticle4.com/review-history/70207>

Original Research Article

Received 20 April 2021
Accepted 25 June 2021
Published 26 June 2021

ABSTRACT

Objective: To determine the risk factors and outcome of acute poisoning in children at a tertiary care hospital of Karachi.

Study design: Cross sectional study

Place and duration of study: Department of Emergency Medicine, Dr Ziauddin Hospital, Karachi, Pakistan. From January 2019 to January 2021

Methodology: The patients (n=136) were selected of either gender with the precise age group of twelve years. All the patients selected were meeting the inclusion criteria and enrolled with a history of poisoning exposure within 24 hours of arriving at the hospital's emergency department. The name of the toxin, the time since ingestion of the toxic substance, factors prompting coincidental harming like age, ill-advised capacity of hurtful specialists, for example, lamp oil and blanch in soda bottles, simple access of kids to meds utilized by different individuals from the family, mother's schooling, working moms, financial status were completely assembled from the guardians or

*Corresponding author: E-mail: doctorsb78@yahoo.com;

orderlies as referenced in the Performa. In general, people were poisoned primarily from within their own homes. Non-accidental poisoning cases were omitted. SPSS version 22 was used to analyze the data.

Results: Out of 136 patient enrolled in this study mean age was 5.2 ± 2.9 years, 77(56.6%) were male and 59(43.4%) were female and mean time of presentation was 2.3 ± 1.7 hours. Most common risk factor was unsafe storage of chemicals (n=98) (72.1%), followed by education level of mother (n=65) (47.8%), inadequate supervision of child (n=60) (44.1%), non authoritative parenting (n=51) (37.5%), working mothers (n=41) (30.1%), lack of family support (n=30) (22.1%), developmental delay (n=11) (8.1%) and poisonous plant in home garden (n=6) (4.4%). Outcome mainly depends upon type of poisoning and time interval between poisoning and presentation to the hospital, 26 (19.11%) were discharged safely from ER, while 45 (33.08%) admit in wards and 48 (35.29%) were admitted in Intensive Care and 17 (12.5%) were expired in ER.

Conclusion: In this study we have concluded that number of accidental poisoning are often occur in toddler and school going children. The major risk factor of acute poisoning found was unsafe storage or easy accessibility of house hold chemicals, second one was low level of education of parents, than non-authoritative parenting, and working mothers and lack of family support. The outcome mainly depend upon time interval from ingestion of poison to presentation at hospital and type poisonous agent taken, that can lead to the need of specialized care, prolong hospital stay and sometimes results in death of a child.

Keywords: Children; poisoning; accidental; factors; outcome.

1. INTRODUCTION

Poisoning is described as ingesting or otherwise being exposed to a substance or substances that are harmful to one's health [1]. Poisoning, whether accidental or purposeful, is a major public health concern around the world. Unintentional poisoning claimed the lives of 346 000 people globally in 2004, according to WHO figures. 91 percent of these deaths happened in low- and middle-income nations. Over 7.4 million years of healthy life were lost due to unintentional poisoning in the same year (disability adjusted life years, DALYs) [2]. Poisoning is a leading cause of emergency room visits and critical care unit admissions, particularly in underdeveloped nations [3].

The prevalence of childhood poisoning has been observed to range from 0.33 percent to 7.6 percent in various studies. Causes of acute poisoning shows variation due to the variety of factors, including age, gender, education, and cultural background, as well as seasonal fluctuations [4]. Poisoning incidence and forms vary greatly around the world, and are influenced by socioeconomic position, cultural traditions, as well as local industrial and agricultural operations [5]. Most medications and chemical substances are now available in the community as a result of technological advancements and societal development. According to the American Association of Poison Control Centers (AAPCC), more than half of poisonings in children under

the age of six occur. Almost all of these exposures are inadvertent, reflecting young children's proclivity to put everything in their mouth [6-7]. Children between the ages of one and four who are more at risk are masculine, energetic, and exhibit increased finger-mouth activity and/or pica [8-9].

According to published research, the most prevalent poisoning agents in industrialised countries are domestic chemical agents and prescribed pharmaceuticals, while agrochemicals are the most common poisoning agents in poor countries [10]. Pesticides for agricultural usage are widely available, and poisoning from such chemicals is particularly common in rural areas where people rely heavily on agriculture for their livelihood [11].

Types of agents are the most significant distinction between paediatric and adult poisonings. Adults are more likely to be poisoned by psychopharmacologic medicines (sedatives, tranquilizers, and antidepressants), but children are more likely to be poisoned by household and personal care products, as well as plants [12]. More than 90% of hazardous exposures in children occur in the home, and the majority of them are caused by a single substance. The vast majority of exposures occur through ingestion, with a small percentage occurring through dermal, inhalational, and ocular routes.

Poisoning is responsible for 10% of all unintentional injuries in low and middle income

nations, as well as 6% of disability adjusted life years [13]. In high-income countries, pharmaceuticals, home items, pesticides, dangerous plants, and insect and animal bites are at the top of the list, whereas in low-income countries, paraffin and kerosene, drugs, and cleaning chemicals are in order [14]. In a South Asian country, 18.5 percent of acute poisoning in children under the age of five has been observed, with a male predominance of 62.5 percent. Kerosene was shown to be the cause of 24.3 percent of all poisonings in children [15-16].

Poisoning was responsible for about 56 percent of all ED visits in 2008, according to one study, with children under the age of four accounting for nearly half of all ED visits. Approximately 54% of all ED visits were made by boys. 87 percent of those who visited the emergency room were routinely discharged, while 7.3 percent were admitted to the same hospital [17].

Accidental poisoning was the most common cause of poisoning in children under the age of 18 in all age groups (72.9 percent), although purposeful poisoning increased with age (p 0.001). Females were also more likely than males to be deliberately poisoned (p 0.001). Drugs were the most common cause of poisoning (41.7 percent). 62.7 percent of deliberate poisoning patients had seen a psychiatrist, with adjustment disorder being the most prevalent diagnosis (44.6 percent) [18]. The majority of the cases (52, 50.5 percent) were purposeful poisoning, whereas 28 (27.2 percent) were unintentional poisoning. Household cleaning chemicals (43, 41.7 percent), organophosphates (28, 27.2 percent), and medicines were the most common causes of poisoning (13, 12.6 percent). The most common presenting symptoms were diarrhoea and vomiting (49.5%), altered consciousness (16.5%), and epigastric discomfort (13.6%) [19].

The importance of this issue is mostly due to the factors that predispose to acute unintentional poisoning. These determinants are numerous, encompassing both situational (geographic location, social and economic constraints, and culture) and individual-related aspects (personality, lifestyle, parenting style, and education level of parents). In an Asian study, maternal employment and a history of poisoning were found to be substantial risk factors for unintentional poisoning in children, but poison availability was found to be a protective factor. Poor maternal education, insufficient child

supervision, substance addiction, and mental illness in family members are all risk factors for poisoning in children, according to the same study [20]. Safe storage and health education on substance abuse prevention were identified as effective interventions for minimising the risk of unintentional poisoning among children in the study community. In the South Asian region, there is a dearth of literature on the risk factors for acute poisoning in children [21]. Ahmed and his colleagues (2011) examined a wide range of poisoning risk factors in Pakistani children, with a particular focus on population-attributable risk variables for acute poisoning. Based on their epidemiological study in India, Agarwal et al. [22] advised that the public be educated on poisoning prevention [22,23].

However, there is no research on the relationship between the length of hospitalisation and the kind of poisoning (pharmaceuticals or non-pharmaceuticals) in children. The American Association of Poison Control Centers (AAPCC) divides the severity of the outcome into five categories:

1. No Effect: The patient did not develop any sign and symptoms.
2. Minor Effect: The patient develop sign and symptoms but resolve rapidly without residual disability and disfigurement.
3. Moderate Effect: Patient develop sign and symptoms secondary to exposure prolonged and more systemic in nature, require treatment but not life threatening.
4. Major Effect: Patient develop life threatening symptoms, lead to disability and disfigurement.
5. Death [24].

2. METHODOLOGY

A cross-sectional study was devised and carried out at Dr Ziauddin Hospital's Pediatric Emergency Department in Karachi, Pakistan. The hospital is a private sector teaching institute and hospital that provides health care to a vast population in Pakistan's Sindh province, both urban and rural. A total of 136 children under the age of twelve who arrived at the pediatric emergency department within twenty-four hours after an accidental hazardous substance exposure were included in the study using a non-probability consecutive sampling technique. Non accidental poisoning cases, such as suicide, iatrogenic drug overdosing, acute food poisoning, a history of snake bite, scorpion or bug sting, dog bite, rat bite, and a hazy history of poisoning,

were all eliminated from the study. Children who met the inclusion criteria for acute poisoning were enrolled in the study after arriving at the emergency department. Questions were asked of parents or attendants about the name of the poison, the amount taken, the time since exposure to poison, and factors leading to accidental poisoning such as age and improper kerosene storage. After the emergency management, patients were followed up on until they were discharged or died. Parents of children with a guarded/poor prognosis will be contacted 4 to 6 weeks following the final outcome, or those who died during treatment, for recruitment into the study. This data was gathered by the lead researcher or on-duty doctor and entered into a pre-designed Performa. SPSS version 22 was used to analyze the data. To determine the importance of the findings, appropriate tests of significance were used.

3. RESULTS

A total of 136 patients were enrolled in this study. Mean age of enrolled participants was 5.2 ± 2.9 years. Among those 77(56.6%) were male and 59(43.4%) were female. Mean time of

presentation in emergency department from exposure to a toxic substance was 2.3 ± 1.7 hours.

Most common agent unintentionally taken by children was hydrocarbons (kerosene oil) 36 followed by organophosphate poisoning 26, psychiatric medications was 14, potassium hydroxide 8, followed by paracetamol 7, and carbon monoxide 1 and miscellaneous substances were 44 that couldn't identified Fig.1.

Regarding clinical presentation, the most common complaint was drowsiness (n=76) (55.88%) followed by epigastric pain and frothing/vomiting (n=60) (44.11%). Common risk factor for acute poisoning was unsafe storage of chemicals (n=98) (72.1%) of cases, followed by education level of mother (n=65) (47.8%), inadequate supervision of child (n=60) (44.1%), non authoritative parenting (n=51) (37.5%), working mothers (n=41) (30.1%), lack of family support (n=30) (22.1%), developmental delay (n=11) (8.1%) followed by poisonous plant in home garden (n=6) (4.4%) Table 1.

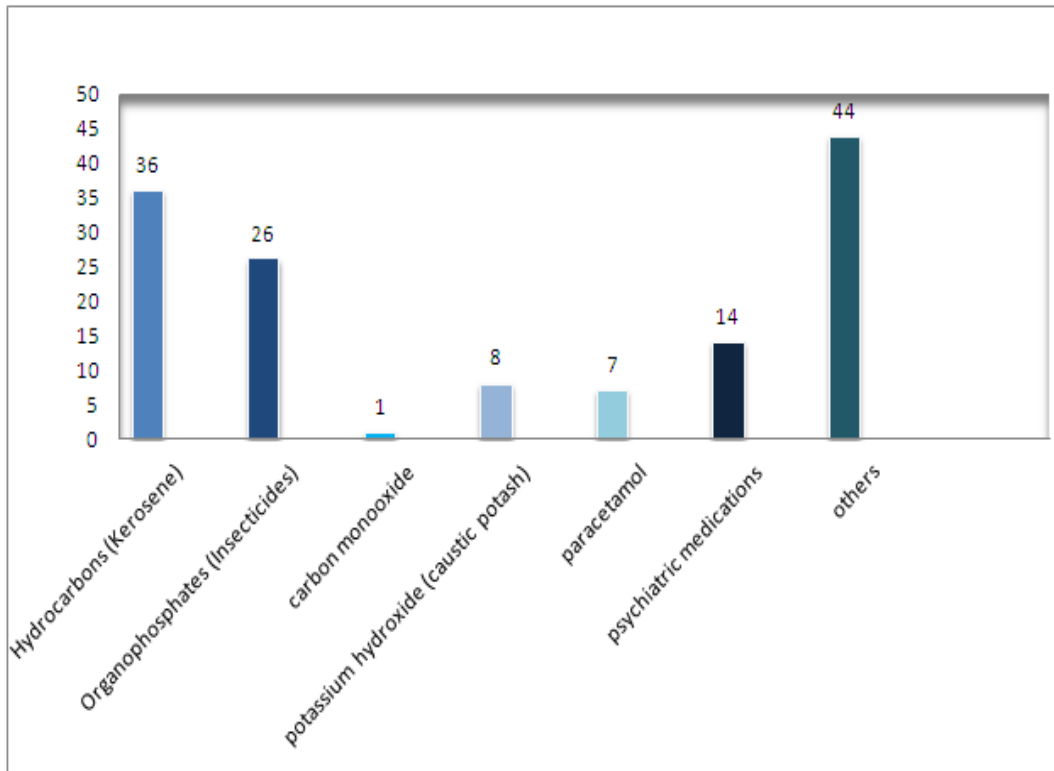


Fig. 1. Type of Poisoning

Table 1. Risk factors for poisoning

Risk factors	Frequency		Percentage %	
	Yes	No	Yes	No
Unsafe storage of household chemicals	98	38	72.1	27.9
Inadequate supervision of the child	60	76	44.1	55.9
Poisonous plants in the home garden	6	130	4.4	95.6
Mother working during the daytime	41	95	30.1	69.9
Non-authoritative parenting style	51	85	37.5	62.5
Primary education level of mother	65	71	47.8	52.2
Lack of family support	30	106	22.1	77.9
Developmental delay in child	11	125	8.1	91.9

Various epidemiological parameters were analyzed to test the association with expected outcome as presented in Fig. 2 and Table 2. Among various parameters, type of poisoning

and time interval between poisoning and presentation to our hospital were significantly different between survived and expired cases.

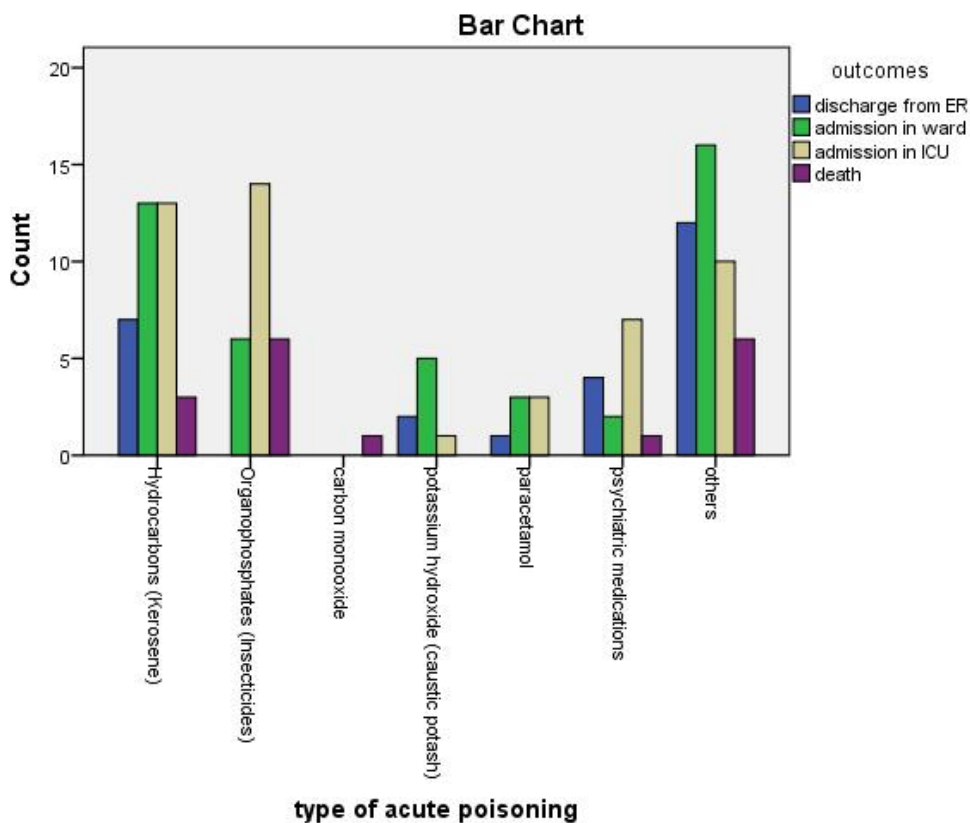


Fig. 2. Relationship between type of poisoning and outcome

Table 2. Duration between exposure and presentation with different outcomes

Duration between exposure and presentation	Outcomes				Total
	Discharge from ER	Admission in ward	Admission in ICU	Death	
.50	1	7	5	3	16
1.00	5	4	11	3	23
1.50	5	5	2	2	14
2.00	6	15	12	5	38
2.50	0	1	1	0	2
3.00	6	7	5	1	19
4.00	2	4	6	2	14
5.00	0	1	2	0	3
6.00	1	0	3	1	5
12.0	0	1	1	0	2
Total	26	45	48	17	136

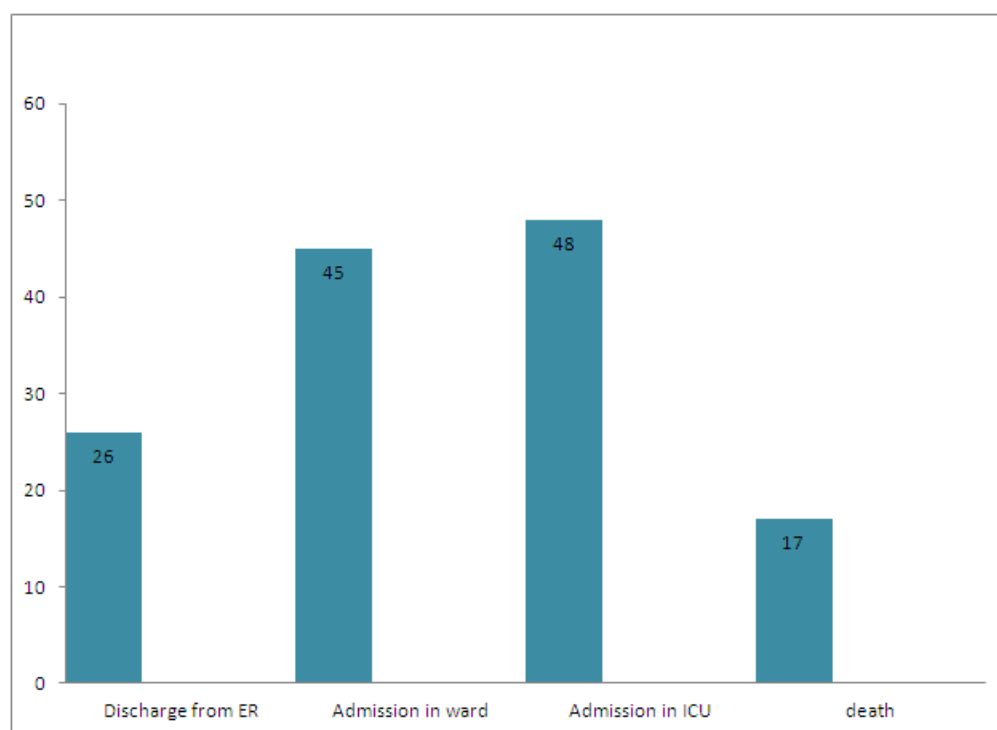


Fig. 3. Outcome of poisoning cases in ER

Out of total number of patients enrolled in the study 26 (19.11%) were discharged safely from ER, while 45 (33.08%) with mild symptoms admit in wards and 48 (35.29%) patient with severe symptomatology were admitted in Intensive Care and 17 (12.5%) were expired in ER, Fig. 3.

3. DISCUSSION

Accidental poisoning in children is one of the leading causes of emergency admissions

globally. In this study, potential causes that lead to acute poisoning in children and their outcomes at the level of the emergency department were examined, and it was determined that these factors can be avoided with suitable preventative measures.

The rate of intoxication in children under 12 represents about 2.4% of the total number of children present in emergency rooms. In a similar study done at hospital of Nepal, 4.0% of total

medical admissions were due to poisoning and 1.0% of pediatric admissions were due to poisoning [25]. In a similar research conducted in India, poisoning accounted for less than 1% of all paediatric admissions under the age of 12 years [26]. In our study we have found that the mean age of acute accidental poisoning is 5 years. A two-year prospective research conducted in Oslo found that 81.0 percent of all poisonings in children under the age of eight were unintentional [27]. This greater rate of unintentional poisoning could be attributed to young children's inquisitive activities. A young child's very nature predisposes him or her to investigate the world around them. Children are impelled to discover new and intriguing items, locations, and objects as they grow and learn to be self-sufficient.

The most prevalent poisoning in our study was caused by hydrocarbons (kerosene oil), followed by pesticides (organophosphates), psychiatric medicine, caustic potash, paracetamol, and miscellaneous. According to a study conducted by Singh et al. in India, hydrocarbons were responsible for 25.3 percent of all childhood poisonings [25]. Hydrocarbons were the agents of poisoning in only 0.9% case in study performed in Columbia [28]. In investigations conducted in Australia and Columbia, organophosphorus poisoning was found in only 2.4 percent and 4.0 percent of youngsters, respectively [29-30]. OP poisoning accounted for 10.1 percent of all childhood poisoning in an Indian study [25]. Poisoning by hydrocarbons was shown in our study to be caused by the use of kerosene oil in normal home activities, which is typically stored in soft drink bottles that attract youngsters.

In our study most common risk factor of poisoning in found to be unsafe storage of household chemicals followed by primary level of education of mother, inadequate supervision of child, non-authoritative parenting style, mother working in day time, lack of family support, mental health of child and present of poisonous plant in home garden. Another study found that cases had more improper storage of household chemicals and medications than controls³⁰. The mother's educational status has a considerable impact on the occurrence of poisoning in children. Most studies found that the majority of mothers were uneducated; in our study, 47.58 percent of mothers had just a primary level of education or were ignorant, resulting in increased morbidity and death in these children. Acute

unintentional poisoning is also linked to factors like as working mothers and a lack of family support.

Different clinico-epidemiological factor are also analyzed to find association with final outcome in emergency department. A total of 136 patients visited the ER included in the study out of which, 48 was admitted in Intensive care area, 45 admit in wards, 26 safely discharged after emergency management and 17 patient were expired. Among which time from exposure to presentation in ER shows significant association with poor outcome. A study conducted in India found that the time between poisoning and presentation to the hospital, as well as the length of hospital stay, were significantly different between survivors and those who died [31]. Another factor is type of poison or agent taken insecticides (organo-phosphates) shows highest percentage of mortality in our study 4.41%, kerosene oil 2.20%, with unidentified agents is 4.4%, in contrast study the mortality rate in organo-phosphates, mushroom and organochlorine poisoning were 7.3%, 30.0% and 20.0% respectively [31]. Symptomatology at the time of presentation also shows some impact on outcome of patients.

The findings of this study are very useful for public health since they imply that by managing several previously identified household environmental factors, it is possible to prevent a number of acute unintentional poisoning cases. Despite the study's shortcomings, we need more community-based research over a longer period of time to offer a recommendation for preventing these types of accidents.

4. CONCLUSION

In this study we have concluded that number of accidental poisoning are often occur in toddler and school going children. The major risk factor of acute poisoning found was unsafe storage or easy accessibility of house hold chemicals, second one was low level of education of parents, than non-authoritative parenting, and working mothers and lack of family support. kerosene oil was found to be the most common cause of acute poisoning followed by organo-phosphate, than medicine (sedative and anti psychotics). and other miscellaneous agents i.e silica gel, bleach, acid etc. The outcome mainly depend upon time interval from ingestion of poison to presentation at hospital and type poisonous agent taken, that can lead to the need of specialized care, prolong hospital stay and

sometimes results in death of a child cause severe mental trauma to the family.

It is suggested that proper preventive health care initiative should be taken like formation of the poison information and control centers, starting parental counseling programs in all well bay clinics and outpatient departments of all primary and tertiary care hospitals and also via print and electronic media.

CONSENT

Informed consent was taken from parents or immediate attendants available with the child.

ETHICAL APPROVAL

Approval has been taken from Ethical Review Committee of the institute.

ACKNOWLEDGEMENT

Authors are grateful to staff of department of Pediatrics for their support during the study period regarding collection of data and the patients and their parents took part in the study.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Chandha I A. Poisoning. Indian Journal of Anaesthesia, October 2003;47(5):402-411.
2. WHO. The intentional program on chemical safety (IPCS) -poisoning prevention and management; 2010.
3. Zöhre E, Ayrik C, Bozkurt S, Kose A, Narci H, Cevik I, et al. Retrospective analysis of poisoning cases admitted to the emergency medicine. Arch Iran Med. 2015;18:117-122.
4. Sahin S, Carman KB, Dinleyici EC. Acute poisoning in children; data of a pediatric emergency unit. Iran J Pediatr. 2011;21(4):479-84.
5. Hassan BA, Siam MG. Patterns of acute poisoning in childhood in Zagazig, Egypt: an epidemiological study. Int Sch Res Notices. 2014;2014:245279.
6. Blake D, Dalton S, Gunja N. Transporting children with toxicological emergencies. Emerg Med Australas. 2014;26(3):279-85.
7. Sadeghi-Bojd S, Khajeh A. Chronological variations of children poisoning causes in Zahedan, South of Iran. International Journal of High Risk Behaviors and Addiction. 2014;3(3).
8. Moazzam M, Al-Saigul AM, Naguib M, Al Alfi MA. Pattern of acute poisoning in Al-Qassim region: a surveillance report from Saudi Arabia, 1999-2003. East Mediterr Health J. 2009;15:1005-1010.
9. Pokhrel D, Pant S, Pradhan A, Mansoor S. A comparative retrospective study of poisoning cases in central, zonal and district hospitals. Kathmandu University Journal of Science, Engineering and Technology. 2008;1:40-48.
10. Sheetu MK, Naik JD, Thakur MS, Langare SD, Pandey VO. Retrospective analysis of poisoning cases admitted in a tertiary care hospital. International Journal of Recent Trends in Science and Technology. 2014;10:365-368.
11. Naveen N, Madhuvardhana T, Arun M, Balakrishna Rao AJ, Kagne RN. Profile of suicidal poisoning in Puducherry area. International Journal of Recent Trends in Science and Technology. 2015;14:76-79.
12. Kumar MR, Kumar GP, Babu PR, Kumar SS, Subrahmanyam BV, Veeraprasad M, et al. A retrospective analysis of acute organophosphorus poisoning cases admitted to the tertiary care teaching hospital in South India. Ann Afr Med. 2014;13(2):71-5.
13. Taft C, Volkaner M, Sarmerick S, Freick N. Childhood unintentional injury worldwide: meeting the challenge. American Pediatr Emerg Care. 2010;21:248-51.
14. WHO. Global Burden of Disease: 2004; 2008.
15. Raed M Alazab, Mahmoud T Elmougy, Ramadan A Fayad, Hoda F Abdelsalam, Amr S Mohamed. Risk factors of acute poisoning among children: A study at a poisoning unit of a university hospital in Egypt. N South East Asia Journal of Public Health. 2012;2(2):41-47.
16. Kariyappa M, Benakappa A, Kejjaijah AK, Saraswathipura R. Spectrum of Poisoning in Children: Study from Tertiary Care Hospital in South India. Journal of Evidence based Medicine and Healthcare. 2015;2(33):4989-99.
17. Nalliah RP, Anderson IM, Lee MK, Rampa S, Allareddy V, Allareddy V. Children in the United States make close to 200,000 emergency department visits due to

- poisoning each year. *Pediatric emergency care*. 2014;30(7):453-7.
18. Kim DY, Kim JH, Paik JH, Han SB, Jung HM. Analysis of Characteristics in Children and Adolescents with Poisoning at Emergency Department. *Journal of the Korean Society of Clinical Toxicology*. 2017;15(2):140-7.
 19. Teklemariam E, Tesema S, Jemal A. Pattern of acute poisoning in Jimma University Specialized Hospital, South West Ethiopia. *World journal of emergency medicine*. 2016;7(4):290.
 20. Mansori K, Soori H, Farnaghi F, Khodakarim S, Mansouri S, Hanis, Khodadost M. "A case-control study on risk factors for unintentional childhood poisoning in Tehran," *Journal of the Islamic Republic of Iran*. 2016;30–355.
 21. Ahmed B, Fatmi Z, Siddiqui AR. "Population attributable risk of unintentional childhood poisoning in Karachi Pakistan," *PLoS ONE*. 2011;6(10). Article ID: e26881.
 22. Agarwal G, Bithu K, Agarwal R. "An epidemiological study of acute poisoning in children in a tertiary care hospital of western Rajasthan, India," *International Journal of Contemporary Pediatrics*. 2016;1249–1251.
 23. Dayasiri MB, Jayamanne SF, Jayasinghe CY. Risk factors for acute unintentional poisoning among children aged 1–5 years in the rural community of Sri Lanka. *International Journal of Pediatrics*. 2017;2017.
 24. David DG, James BM, Daniel AS, Daniel EB, Michael OF, William B. 2016 Annual Report of the American Association of Poison Control Centers' National Poison Data System (NPDS); 2017.
 25. Opawoye AD, Haque T. Insecticide/organophosphorus compound poisoning in Children. *Ann Saudi Med*. 1998;18:171-72.
 26. Singh S, Singhi S, Sood NK, Kumar L, Walia BNS. Changing pattern of childhood poisoning (1970-1989): experience of a large north Indian hospital. *Indian Pediatr*. 1995;32:331-6.
 27. Erguvan M, Yilmaz O, Devenci M et al. Mushroom poisoning. *Indian J Pediatr* 2007; 74: 847-57.
 28. Wilkerson R, Northington LD, Fisher W. Ingestion of toxic substances by infants and children. What we don't know can hurt. *Crit Care Nurse* 2005;25: 35–44.
 29. Pathak UN, Chhetri PK, Dhungel S, et al. A retrospective study of poisoning cases admitted in Nepal Medical College Teaching Hospital. *Nepal Med Coll J*. 2001;3:101-5.
 30. O'connor PJ. Differentials in poisoning rates of young Australian children according to residential location and geographical remoteness. *Injury prevention*. 2005;11(4):204-206.
 31. Budhathoki S, Poudel P, Shah D, Bhatta NK, Dutta AK, Shah GS, Bhurtyal KK, Agrawal B, Shrivastava MK, Singh MK. Clinical profile and outcome of children presenting with poisoning or intoxication: a hospital based. study. *Nepal Med Coll J*. 2009;11(3):170-5.
 32. Beautrais AL, Fergusson DM, Shannon FT: Accidental poisoning in the first three years of life. *Journal of Paediatrics and Child Health*. 2008;17(2):104-109.

© 2021 Qureshi et al.; This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Peer-review history:

The peer review history for this paper can be accessed here:
<http://www.sdiarticle4.com/review-history/70207>