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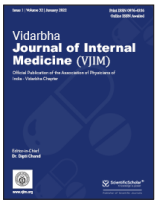

Original Article

Clinical Profile and in Hospital Outcome of Acute Poisoning Cases Admitted in Tertiary Care Hospital: A Prospective Observational Study

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ABSTRACT

Objectives: Acute poisoning is a medical emergency. Data are scarce from the Indian subcontinent regarding the profile and outcome of patients presenting with acute poisoning admitted to intensive care unit (ICU). Hence, the present study was undertaken to assess the clinical profile and hospital outcome of acute poisoning cases admitted in tertiary care hospitals.

Material and Methods: A total of 148 patients with acute poisoning aged >18 years and admitted in the intensive care unit and medicine wards of tertiary care hospital during a period of 1 year from September 1, 2019, to August 31, 2021, were studied.

Results: Poisoning was more common in the 21–30 years age group (42.57%) with male predominance (55.41%). Poisoning with suicidal intention constituted 81.76%: 44.59% of cases seeking medical help within 2–4 h. In 81.76% of cases, route of poisoning was oral. Organophosphorus was the most common acute poisoning (28.38%), and most common symptoms were nausea/vomiting. Complications noted were ventilator-associated pneumonia (VAP) (4.72%), renal failure (6.08%) and hepatic failure (2.7%). Mortality was seen in 11.49% of cases. Out of 148 cases, 121 were of suicidal poisoning, while 14 patients out of them expired so psychiatric evaluation of 107 patients can be made and out of that all patients had some underlying psychiatric illness. Patients requiring ventilatory support constituted 25.67% of cases.

Conclusion: Clinical profile of acute poisoning depends on the nature of compound/poison, quantity of compound consumed/exposed, first aid received at the primary care level and time taken to shift the patient from primary care level to tertiary care level. In-hospital mortality mostly depends on the dedicated facilities available at the tertiary care level in addition to the factors described above for clinical profile.

Keywords: Acute poisoning, Clinical profile, Organophosphorus, Mortality, Psychiatric

INTRODUCTION

Acute poisoning due to suicidal or accidental exposure causes significant mortality and morbidity throughout the world. It has become a common method of deliberate self-harm.[1] According to the legal system of our country, all poisoning death cases are recorded as unnatural death and a medico-legal autopsy is routine.[2] It is a major problem in India which accounts for 29.1% of all suicidal deaths. The nature of the poison used varies in different parts of the world, and different parts of the same country. It is a major problem in India.[3]

The pattern of poisoning in a region depends on various factors such as availability, access to the poison, socio economic status of the individual, and cultural and regional influences. High doses of analgesics, tranquillizers and antidepressants are the commonly used agents for intentional poisoning in developed countries and pesticides are used commonly in Asian regions for self-poisoning particularly in rural areas.[4] Rapid industrialisation, introduction of newer range of drugs for treatment and extensive use of pesticides in agriculture have increased the incidence of poisoning. Over the past few decades, agricultural pesticide has become a common household item in rural areas of developing world.[5]

The severity and outcome in such cases are determined by several factors such as chemical and physical properties of the poison, amount consumed, mode of poisoning, pre-existing disease and most importantly treatment initiation.[6] Early medical intervention such as initial resuscitation, gastric lavage and use of specific antidotes improves the outcome.

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Specific antidotes for all poisonings are not always available, neither are proper treatment protocols followed. Hence, the present study was conducted to provide knowledge about the nature and magnitude of the problem in this particular area, thus helping in the early diagnosis and treatment of the cases. The other objectives were to assess the clinical profile and hospital outcome of acute poisoning cases admitted in tertiary care hospitals.

MATERIAL AND METHODS

After obtaining Institutional Ethical Committee approval and written informed consent from patients/relatives, this prospective observational study was conducted on 148 patients with acute poisoning aged >18 years and admitted in the intensive care unit and medicine wards of the tertiary care hospitals of central India during a period of 1 year from September 1, 2019, to August 31, 2021. Patients not willing to enrol/not given consent, age <18 years, idiosyncratic reaction to drugs, cases of acute ethyl alcohol intoxication, cases of envenomation by bite or sting and cases of food poisoning were excluded from the study.

A detailed history was taken, and sociodemographic variables were noted. Furthermore, nature of poison (Trade name and chemical name of compound, class of compound), presenting complaints, first aid/treatment received at primary level, time lag from exposure to the first aid and time lag from first aid to tertiary hospital were recorded. General examination included smell of poisonous compound, temperature of patients, pulse (rate, rhythm, volume and character), respiration, type of breathing, tachypnoea, dyspnoea, blood pressure, pallor, icterus, cyanosis, pupils, fasciculation, skin examination (excessive sweating/dry), signs of burns at lips/buccal mucosa (in case of corrosive compound poisoning) – salivation, Oxygen saturation, jugular venous pressure and oedema feet were noted at the time of admission. Systemic examination (CVS), respiratory system, abdominal and CNS examination were done. Routine investigations Complete Blood Count, Liver Function Test, Kidney Function Test, Peripheral Smear, Random Blood Sugar, Urine Routine Microscopy, X ray Chest and special investigations (Serum cholinesterase, Arterial Blood Gas, serum and plasma levels of drugs (if feasible and available), Computed tomography scan (if indicated) and Magnetic Resonance Imaging (if indicated) were carried out. The treatment for any poisoning was carried out according to standard protocols. Complications if any were noted and managed with haemodialysis/peritoneal dialysis, ventilatory support and temporary pacing. In hospital outcomes, that is, discharge and death were noted. Total duration of hospital and intensive care unit stay was recorded. A detailed psychiatric evaluation was done to find out underlying/precipitating cause of poisoning.

Data analysis

Data were analysed using statistical software STATA version 10.1, 2011. Descriptive statistics are calculated to summarize quantitative variables by mean and standard deviation and qualitative variables by frequency and percentages. Proportion expressed as percentage (point estimate, along with 95% confidence interval (Interval estimate). Inferential statistics include Chi-square test and *t*-test for assessing significance of differences in proportions by various subgroups o strata of baseline characteristics (such as age, gender and other demographics). $P < 0.05$ was considered statistically significant.

RESULTS

Most of the cases were aged between 21 and 30 years (42.57%), male gender (55.41%), belonging to lower-socioeconomic class (70.27%), farmer (31.08%) from rural areas (64.87%), married (58.18%) and had completed high schooling (33.11%), as shown in [Table 1].

At the time of admission, 22 (14.86%) cases out of 148 were presented with constricted pupils, about 34 (22.97%) patients were having fasciculations and signs of skin burns were there in 8 (5.41%) patients, while 11 (7.48%) patients having signs of mucosal burns, 35 patients presented with excessive salivation and other increased tendency of secretions.

Out of total of 148 subjects studied, 131 (88.51%) patients survived and were discharged from hospital, while 17 patients (11.19%) expired which was statistically highly significant, ($P < 0.001$) [Figure 1].

Poisoning with suicidal intention constituted 81.76% of cases: 44.59% of cases seeking medical help within 2–4 h. Twelve patients (8.11%) attended after 8 h of poisoning having maximum mortality of 33.33%. One hundred and twenty-three patients (86.99%) received stomach wash of them 107 survived (86.99%). Maximum mortality (60%) seen in aluminum phosphide compound (celphos) poisoning. In most of the cases (85.14%), route of poisoning was oral. Most of the patients were conscious (76.35%) at presentation, whereas 7.43% of cases were unresponsive, as shown in [Table 2].

[Table 3] shows the comparison of mean values of baseline haemodynamic and laboratory parameters and outcomes of patients. The mean value of SpO_2 among non-survivors was less than the survivors which was statistically highly significant, ($P < 0.001$).

Out of 148 cases studied, 38 (25.68%) require ventilatory support, among them 21 survived and 17 patients expired which was statistically highly significant, (<0.0001). Seventy-three patients needed ICU care. Mean ICU stay among survivors was 4.63 ± 2.49 days, while, in non-

Table 1: Sociodemographic profile of poisoning patients.

Parameters	Number of cases	Percentage
Age in years		
≤20	25	16.89
21–30	63	42.57
31–40	27	18.24
41–50	15	10.14
51–60	10	6.76
>60	08	5.41
Gender		
Male	82	55.41
Female	66	44.59
Marital status		
Single	65	43.99
Married	83	56.01
Domicile		
Urban	52	35.13
Rural	96	64.87
Education		
Illiterate	15	10.13
Primary schooling	19	12.84
Middle schooling	27	18.24
High schooling	49	33.11
Graduate	24	16.22
Post-graduate	14	9.46
Occupation		
Farmer	46	31.08
Housewife	27	18.24
Labourer	22	14.86
Student	21	14.19
Govt. employee	07	4.73
Dependent	02	1.35
Others/unemployed	23	15.55
Socioeconomic class		
Upper class	06	4.05
Upper middle	13	8.78
Lower middle	25	16.9
Upper lower	36	24.32
Lower	68	45.95

survivor, it was 4.97 ± 4.023 days. Maximum mortality was among the patients with ICU stay of 3–7 days. However, the mean hospital stay among survivors was 7.92 ± 5.18 days and, in non-survivor, it was 6.37 ± 4.02 days. Maximum mortality was among the patients with hospital stay of 8–11 days. Complications noted were ventilator-associated pneumonia (VAP) (4.72%), renal failure (6.08%) and hepatic failure (2.7%), as shown in [Table 4].

Out of total of 148 cases, 121 cases were of suicidal poisoning, while 14 patients out of them expired so psychiatric evaluation of 107 patients can be made and out of that all patients had some underlying psychiatric illness, most common was impulsive (35 cases) and adjustment disorder (30 cases), as depicted in [Figure 2].

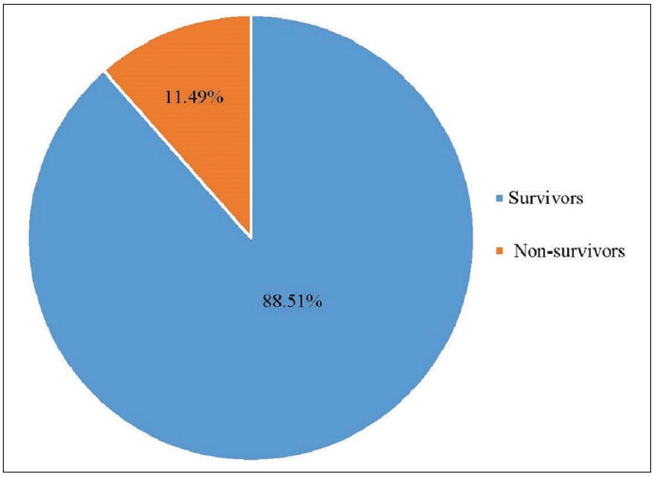

Figure 1: In hospital outcome of acute poisoning cases.

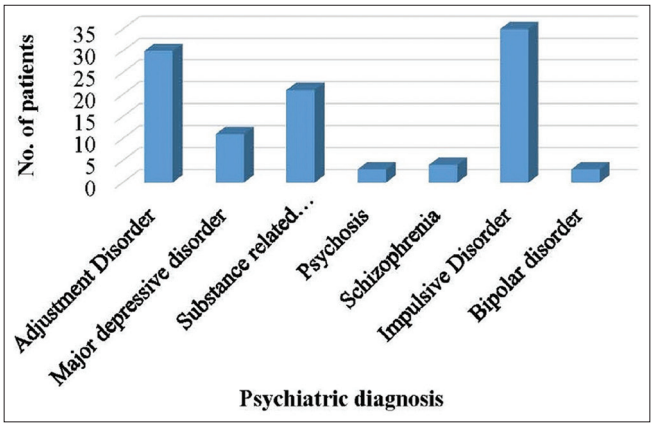

Figure 2: Psychiatric diagnosis.

DISCUSSION

In the present study, more poisoning cases were seen in the third decade of life which is comparable with the previous studies,[7-9] probably due to modern lifestyle, unemployment, failure in love, failure in education, family problem, impulsive behaviour, work pressure, interpersonal relationships, marriage and an immature mental framework. Poisoning among males was more (55.41%) similar to other studies.[6,7] This could be because men had more access to poisons and were also susceptible to the stress and strain of day-to-day life. We had a greater number of accidental poisoning cases in males as compared to females. Majority of these cases were from rural areas, so probably inhalation of poison could have happened during spraying on crops. This maybe because of widespread use of pesticides in agriculture sector in rural areas. Poverty, failure of crops, family problems and easy availability of the poison in their household made people of rural areas more prone to poisoning. Other studies also show that poisoning is more common in rural areas.[9,10] As similar to another study,[9]

Table 2: Association of various study parameters with outcome.

Parameters	Total (%)	Survivors (%)	Non-survivors (%)	*P*-value (%)
Time delay (In hours)				
<2	46 (31.08)	43 (93.48)	03 (6.52)	0.020
2–4	66 (44.59)	61 (92.42)	05 (7.58)	
5–8	24 (16.22)	19 (79.17)	05 (20.83)	
>8	12 (8.11)	08 (66.67)	04 (33.33)	
Stomach wash				
Given	123 (83.10)	107 (86.99)	16 (13.01)	0.198
Not given	25 (16.89)	24 (96.0)	01 (4.0)	
Type of poisoning				
Suicidal	121 (81.76)	107 (88.43)	14 (11.57)	0.946
Accidental	27 (18.24)	24 (88.89)	03 (11.11)	
Compound consumed				
Organophosphate	42 (28.38)	37 (88.10)	05 (11.90)	<0.001
Drug overdose	22 (14.86)	21 (95.45)	01 (4.55)	
Unknown compound	20 (13.51)	18 (90.0)	02 (10.0)	
Corrosives	19 (12.84)	19 (100)	00 (0.0)	
Rat killer compound	16 (10.81)	15 (93.75)	01 (6.25)	
Other insecticide and pesticide	11 (7.43)	10 (90.90)	01 (9.10)	
Celphos	10 (6.76)	04 (40)	06 (60)	
Carbamate	08 (5.41)	07 (87.5)	01 (12.5)	
Route of administration				
Oral	126 (85.14)	111 (88.10)	15 (11.90)	0.703
Inhalational	22 (14.86)	20 (90.91)	02 (9.09)	
Crepitation				
Present	40 (27)	23 (17.56)	17 (100)	<0.0001
Absent	108 (73)	108 (82.44)	00 (0.0)	
Consciousness				
Conscious	113 (76.35)	109 (83.21)	04 (23.53)	<0.0001
Drowsy	24 (16.21)	16 (12.21)	08 (47.06)	
Unconscious	11 (7.43)	06 (4.58)	05 (29.41)	

Table 3: Baseline haemodynamic and laboratory parameters and outcome of patient.

Parameters	Survivors	Non-survivors	*P*-value
Baseline haemodynamic parameters			
Pulse rate	79.87±15.88	80.70±3.81	0.8399
Respiratory rate	15.50±2.76	16.0±3.20	0.4952
SpO_2	92.59±10.46	78.94±6.57	<0.0001
Laboratory parameters			
Serum cholinesterase	2737.5±3414.21	2850.5±3424.19	0.3927
Hb	10.16±1.90	11.19±1.62	0.0345
TLC	7644.0±2298.01	6668.65±2185.26	0.1158
Platelet	3.03±1.17	2.92±1.25	0.7103
Urea	28.15±9.35	29.57±10.10	0.5590
Creatinine	0.79±0.17	0.79±0.17	0.9763
Total bilirubin	0.92±1.30	0.91±0.98	0.7103
ALP	182.95±56.92	208.11±56.21	0.0881
SGOT	31.83±13.18	35.82±12.68	0.2411
SGPT	26.94±10.69	24.53±11.56	0.3865
RBS	112.52±21.29	112.76±21.74	0.9645

SPO_2: Oxygen saturation, Hb: Haemoglobin, TLC: Total leucocyte count, ALP: Alkaline phosphatase, SGOT: Serum glutamic-oxaloacetic transaminase, SGPT: Serum glutamate pyruvate transaminase, RBS: Random blood sugar

in the present study married people formed majority of the study subjects. More cases of poisoning were noted in married females (n = 43 [65.15%]), than in unmarried females (n = 23 [34.85%]). Similar results were obtained

Table 4: Complications and its management between survivors and non survivors.

Complications	Survivors (%)	Non-survivors (%)	*P*-value
Complications			
AKI	06 (50)	03 (33.33)	0.034
Hepatic failure	03 (75.0)	01 (25.0)	0.389
VAP	03 (42.86)	04 (57.14)	0.003
No complication	119 (92.97)	09 (7.03)	-
Management of complication			
Conservative	02 (50.0)	02 (50.0)	0.065
Dialysis	04 (80.0)	01 (20.0)	0.462
Higher antibiotics	03 (42.86)	04 (57.14)	0.003
N acetyl cysteine	03 (75.0)	01 (25.0)	0.406

AKI: Acute kidney injury, VAP: Ventilator associated pneumonia

in other studies also.[6,9,10] More frequency of poisoning in married females is common, as they have more responsibility in comparison to unmarried persons, and conflict with their spouse or other family members. About 10.13% of cases were illiterate which is due to fact that majority of patients were from rural areas. Accidental cases of poisoning occur due to illiteracy. This finding also shows that education is important in preventing poisoning. Poisoning was most common in farmers (31.08%), could be due to easy availability and accessibility of poisons, particularly insecticides and pesticides which are comparable with the study done by Khosya and Meena.[10] Thus, farmers and other people involved in spraying insecticides should be educated regarding prophylactic measures. They must be counselled to wear protective garments, not to spray at a stretch for more than 2 h and to avoid food intake in the spraying area. They should also be informed to discontinue spraying on appearance of any of the symptoms and to avoid spraying in presence of any wound. Population from lower socioeconomic status (70.27%) consume poison more frequently than the upper socioeconomic status (4.05%) which was similar finding as other studies.[7,10] Even if the maximum number of acute poisoning cases belong to the lower socioeconomic status and rural areas we cannot dogmatically conclude that the acute poisoning is predominantly in the lower socioeconomic strata and rural areas as most of the patients attending government tertiary care hospital belongs to lower socioeconomic strata are either from rural areas or from urban slum areas and needs to be further evaluated compiling the overall data from government as well as private tertiary care hospitals.

In most of the cases (85.14%), route of poisoning was oral and organophosphorus (OP) compound poisoning was the most common cause of poisoning (28.38%), which is comparable with the earlier studies.[6-10] The previous studies[7,9] show that patient if brought for the treatment early has more chances of survival. Similarly, in the present study, minimum mortality was observed in the group where time interval between primary treatment and referral to tertiary care hospital/directly attending tertiary care hospital was <2 h followed by 2–4 h. Hence, we conclude that the interval between exposure of poison to first aid should be considered as golden hour management and should be preferably <2 h or within 2–4 h, this concept of golden hour management for acute poisoning should be incorporated by National Health Mission program and effectively followed at primary or secondary care level at par with the concept of golden hour management in acute coronary stroke and acute ischemic stroke.

Most of the patients with OP compound consumption were presented with nausea and vomiting, small sized or constricted pupils, excessive salivation and along with fasciculations which comprise largest number of cases which are similar findings as in other studies.[6,8-10] Mortality rate among the OP compound poisoning was 11.90%. In organophosphate poisoning, requirement of ventilator was due to respiratory depression, a complication seen in most organophosphate poisoning cases, while most of them recover after ventilatory support.

A total of 10 (6.76%) subjects with aluminum phosphide poisoning were admitted to the ICU, seven among them had consumed the unexposed form of the tablet which is more harmful. These patients presented with nausea and vomiting. All the patients who consumed the unexposed poison had respiratory distress and arrhythmias, and hypotension, similar findings were noted by Khosya and Meena,[10] and six out of seven of this had to be intubated and one require NIV support, six among them died (case-fatality ratio of 60%). Requirement for ventilator was most commonly associated with aluminium phosphide poisoning because most of the patients with aluminium phosphide poisoning had either severe acidosis or cardiac arrest. Patients with rat killer compound (zinc phosphide) consumption presented most commonly with abdominal pain, followed by palpitation, dyspnoea and shock which are similar to findings from the previous studies.[6,9,10] Mortality rate of rat killer compound was 6.25% which is almost similar to finding by Khosya and Meena (9.6%).[10]

Among the total cases, 76.35% (n = 113) were conscious during the time of presentation, whereas 16.22% (n = 24) of subjects were drowsy and 7.43% (n = 11) were unconscious. A total of 24.32% (n = 36) subjects required endotracheal intubation and two patients require NIV support because of respiratory distress and airway protection. Standard protocols were followed which included the A, B and Cs of emergency management, insertion of Ryle's tube and gastric lavage. Supportive treatment consisted of use of PPI, anti-emetics and IVF. Atropine and pralidoxime were used in poisonings by OP compound. Glycopyrrolate was used to

reduce secretions due to OP poisoning. Specific antidotes were used wherever required.

Treatment included preventing further absorption of the poison, increasing the elimination, and administering specific antidotes to eliminate, counteract or inactivate the effects of the poison, if available. There were 88.51% (n = 131) of subjects who recovered, and 11.49% (n = 17) patients who died due to poisoning, despite adequate management. A similar result was seen in another study by Ali *et al*.[9] and Khosya and Meena.[10]

Almost all patients (121 cases) having suicidal poisoning had some underlying psychiatric illness (107 cases); hence, all patients of poisoning including suspected of accidental poisoning should be subjected to psychiatric evaluation and management before discharge to prevent further suicidal attempts. The concept of Preventive Mental Health with respect to acute poisoning cases needs to be included in the National health mission program and implemented effectively in perspective of acute poisoning.

Duration of hospital stay in the present study ranged from 1 to 28 days and mean duration of stay was 6.77 ± 4.38 days. Minimum hospital stay was found for aluminium phosphide (3.9 ± 2.13 days), followed by corrosive poisoning (4.52 ± 1.46 days), while maximum stay was found for OP compound poisoning (10.07 ± 4.72 days). Similar results were obtained in study done by Ali *et al*.[9] In aluminium phosphide poisoning cases, most of the patients expired within 1–3 days, this is the reason for less hospital stay. OP compound poisoning patients undergo respiratory failure so require ventilatory support and prolonged hospital stay.

CONCLUSION

Clinical profile of acute poisoning depends on the nature of compound/poison, quantity of compound consumed/exposed, first aid received at the primary care level and time taken to shift the patient from primary care level to tertiary care level. In-hospital mortality mostly depends on the dedicated facilities available at the tertiary care level in addition to the factors described above for clinical profile. Minimum mortality observed in our study is in the group, where time interval between primary treatment and referral to tertiary care hospital/directly attending tertiary care hospital is <2 h followed by 2–4 h. Hence, we conclude that the interval between exposure of poison to the first aid should be considered as golden hour management and should be preferably <2 h or within 2–4 h, this concept of golden hour management for acute poisoning should be incorporated by National Health Mission program and effectively followed at primary or secondary care level at par with the concept of golden hour management in acute coronary stroke and acute ischemic stroke.

Almost all patients having suicidal poisoning had some underlying psychiatric illness; hence, all patients with poisoning including suspected accidental poisoning should be subjected to psychiatric evaluation and management before discharge to prevent further suicidal attempts. The concept of Preventive Mental Health with respect to acute poisoning cases needs to be included in the national health mission program and implemented effectively in perspective of acute poisoning. Even if the maximum number of acute poisoning cases belong to the lower socioeconomic status and rural area, we cannot dogmatically conclude that the acute poisoning is predominantly in the lower socioeconomic strata and rural areas as most of the patients attending government tertiary care hospital belongs to lower socioeconomic strata are either from rural areas or from urban slum areas and needs to be further evaluated compiling the overall data from government as well as private tertiary care hospitals. Farmers and other people involved in spraying insecticides should be educated regarding prophylactic measures. They must be counselled to wear protective garments, not to spray at a stretch for more than 2 h and to avoid food intake in the spraying area. They should also be informed to discontinue spraying on appearance of any of the symptoms and to avoid spraying in presence of any wound. Curtailing the sale of over-the-counter medications, preventive measures like restriction of sale of potentially poisonous substances and promoting poison information centres might bring down the incidence of poisoning.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Chatterjee S, Verma VK, Hazra A, Pal J. An observational study on acute poisoning in a tertiary care hospital in West Bengal, India. Perspect Clin Res 2020;11:75-80.
2. Doraickannu T, James J, Sechassayana N. A prospective observational study on poisoning cases in a tertiary care hospital in Tamil Nadu. J Evid Based Med Healthc 2019;6:1203-7.
3. Getie A, Belayneh YM. A Retrospective study of acute poisoning cases and their management at emergency department of Dessie referral hospital, Northeast Etihopia. Drug Healthc Patient Saf 2020;12:41-8.
4. Chelkeba L, Mulatu A, Feyissa D, Bekele F, Tesfaye BT. Patterns and epidemiology of acute poisoning in Ethiopia: Systematic

review of observational studies. Arch Public Health 2018;76:34.
5. Pingali PL. Green revolution: Impacts, limits, and the path ahead. Proc Natl Acad Sci U S A 2012;109:12302-8.
6. Mate VH, Dhande PP, Gonarkar SB, Pandit VA. A Prospective observational study on pattern, severity and outcome of different poisoning cases in a tertiary care hospital, India. J Basic Clin Pharma 2017;8:154-7.
7. Bhadade R, Desouza R, Gangawane S. Analysis of poisoning in urban setting: A single centre study. J Assoc Physicians India 2019;67:57-61.
8. Adinew GM, Woredekal AT, DeVos EL, Birru EM, Abdulwahib MB. Cases of poisoning and their treatment in emergency departments of emergency hospitals in northwestern Ethiopia. Afr J Emerg Med 2017;7:74-8.
9. Ali I, Sawlani KK, Himanshu D, Chaudhary SC, Usman K, Atam V, *et al*. Study of pattern and outcome of acute poisoning cases at tertiary care hospital in north India. J Evid Based Med Healthc 2017;4:326-31.
10. Khosya S, Meena S. Current trends of poisoning: An experience at a tertiary care hospital Hadoti region, Rajasthan, India. J Clin Toxicol 2016;6:298.

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