Original Article

The Relative Risk of Toxico-Clinical Parameters with respect to Poisoning Severity and Outcomes in Patients with Acute Poisoning

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Abstract

Background: Complications or death risk factors is necessary for better monitoring and treatment. The aim of this study was to define the relative risk of toxico-clinical parameters with regard to poisoning severity and outcomes in patients with acute poisoning.

Materials and Methods: This cross-sectional study entailed of patients with acute poisoning admitted to the poisoning emergency center of khorshid hospital, Isfahan, Iran from December 2018 until March 2019. Patients (n = 300) were categorized into four groups (minor, moderate, severe, and fatal poisoning) based on severity. Multivariate logistic regression analysis was employed to calculate the odds ratio (OR) as the estimate of the relative risk of the different variables for the poisoning severity and outcomes prediction.

Results: In the minor group, opioids/opiates, alcohols, and benzodiazepines (14.7%) were the most prevalent poisoning, multidrug (23.3%) was in the moderate and severe groups and finally, pesticides poisoning (23%) was most common in the fatal group. The predictive factors for poisoning severity were pre-hospital antidote administration [OR, (95%CI); P value] [7.08 (1.77-28.34); 0.006]; loss of consciousness [4.38 (1.84-10.42), 0.001]; abnormal ECG [4.56 (1.65-12.56); 0.003]; and time interval of poisoning to admission in the hospital [1.15 (1.02-1.28); 0.01). Patients without complications was observed in 49.7% of subjects. Patients with the loss of consciousness [66.06 (2.41-180.07); 0.01); underlying disease [3.65 (1.09-12.24); 0.03]; abnormal respiration [1.14 (1.02-1.27); 0.02); have had a greater risk of complications and death.

Conclusion: Important factors for poisoning severity and/or outcome were loss of consciousness, pre-hospital antidote administration, abnormal ECG or respiration, underlying disease, and delay to presentation to hospital.

Keywords: Complication, death, epidemiology, outcome, poisoning, severity score

INTRODUCTION

Acute poisonings are one of the important medical emergencies considered as an epidemic worldwide.[1] A total of 168,000 people die from suicide with pesticides every year in developing countries.[2] Estimations based on a systematic review showed that 385 million cases of unintentional, acute pesticide poisoning happen annually worldwide, consisting of around 11,000 mortalities.[3] Furthermore, drug poisonings have also increased during the years showing more serious outcomes.[4] In addition, the incidence of poisoning may be greater in some countries due to a lack of monitoring systems with incomplete regulations, an absence of training, insufficient availability of information systems, and large agricultural-based populations.[2]

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Complications or death risk factors in patients with acute poisoning are necessary for better monitoring and treatment. Usually, the different scoring systems used in the emergency room selecting patients for the hospitalization intensive care unit (ICU). Clinicians with recommended criteria could predict poisoning outcomes, qualitative assessment of the disease, and evaluation of poisoning patterns in patients.[5-7] Poisoning severity score (PSS) is one of these criteria reported by Persson *et al*. in 1998.[8] PSS has been used in identifying the severity of intoxication[8,9] and utilized for critically ill patients to predict the development of their illness. They are also suitable in research when comparing groups of patients.[10] Different studies have shown some factors have been associated with the severity of poisoning, including age, nonaccidentally poisoning, respiratory and circulatory failure, unresponsiveness to treatment and seizures.[11-13] In addition, electrocardiographic (ECG) signs[14,15] and biochemical markers also linked with poisoning severity.[12] Considering the importance of risk factors for outcome prediction in patients with acute poisoning, in a cross-sectional study, we evaluated the relative risk of toxico-clinical parameters on poisoning severity and outcomes in patients with acute intoxication.

MATERIALS AND METHODS

This cross-sectional study was conducted in the referral poisoning emergency center of Khorshid Hospital, affiliated with Isfahan University of Medical Sciences, Isfahan, Iran. The sample size was determined 300 patients using the significant level of 5%; the statistical power of 80% and an effect size of 0.5 (75 patients in each group). The sampling method was nonprobability convenient samplings. The inclusion criteria consisted of patients (adults and children) with acute poisoning, including bites, and other poisoning (drug, opiates/opioids, stimulants, alcohols, and pesticides admitted to the poisoning emergency room from December 2018 until March 2019. Patients with a history of intoxication who were asymptomatic during the observation period in the hospital were excluded from the study. Also, discharge of patients with personal consent and the lack of sufficient data in the medical files were another exclusion criteria. The attending physicians made the diagnosis of poisoning considering the history reported by the patients or their relatives, clinical manifestations, and serological toxicological tests and toxicology urine analysis, if necessary.

The severity of poisoning was determined based on the variables in the PSS.[8] Data were gathered from a review of the case notes of the emergency physicians. Chart abstractor (second author) trained before the study starts, using a set of "practice" medical records. As the asymptomatic patients were excluded, other patients were categorized based on variables in the PSS checklist into four groups; minor, moderate, severe, and fatal poisoning. Demographic data (age, gender, marital status); the history of drug abuse; previous medical or psychiatric diseases; type of poisoning (intentional, accidental, unaware); route of exposure; kinds of poisoning (bites, substances) based on ICD-10 code on the medical records including drug, opiates/opioids, stimulants, alcohols, and pesticides; time to hospital admission; clinical manifestations; ECG changes; therapeutic modalities (prehospital and in-hospital gastrointestinal decontamination, administration of antidote); endotracheal intubation at the time of admission and within 24 h of admission; length of hospital stay and outcome of the patients (recovery without complication, recovery with complications, and death) were recorded in the data collection form. Underlying diseases, including diabetes, cardiovascular disease, chronic renal failure, liver failure, hypertension, respiratory diseases, as well as the history of any psychiatry diseases which was diagnosed and treated by a psychiatrist, was also recorded.

We classified the ECG as normal and abnormal with respect to the age and gender of the patients. Abnormal ECG consisted of tachycardia, bradycardia, arrhythmia, wide QRS complex, QT prolongation, heart blocks, and ST-T changes. Furthermore, based on different age groups (children/adults), patients' respirations were categorized to normal and abnormal respiration. Patients who had an abnormal respiratory rate (tachypnea, bradypnea) and abnormal breathing pattern were included in the "abnormal group."

Treatment modalities were categorized into two groups (pre-hospital and in-hospital). Those patients who had been referred form the other centers and had been received some treatment interventions in other centers before admission to Khorshid hospital were in the "pre-hospital" group. In addition, those who received the treatment modalities only in Khorshid Hospital were in "in-hospital" group.

We ensured the uniform handling of the data collection with the consensus meetings. In addition, periodic meetings with the chart abstractor (second author) and study coordinators (Corresponding author and First author) were held to resolve disputes and review coding rules. The performance of the chart abstractors was monitored by the corresponding author of the research project.

Data are presented as mean ± standard deviation, median (Minimum-maximum), and frequency (percentage) as appropriate. We used Chi-square/Fisher's exact tests and ANOVA for analysis. The *post hoc* analysis was performed using Tuckey's test. In addition, multivariate logistic regression analysis was used to calculate the odds ratio (OR) as the estimate of the relative risk of the different variables for the poisoning severity and outcomes prediction. All toxico-clinical variables which were significantly different between groups based on univariate analyses ($P < 0.05$) were included for multivariate logistic regression analysis. Recovery with complications and death combined as a single ordinal variable, comprising two possible outcomes: (0) recovery without complication, (1) complication and death. The $P < 0.05$ were considered statistically significant. All statistical analyses were conducted using SPSS software version 15 (SPSS Inc., Chicago, IL, USA).

RESULTS

Out of 300 patients included during the study period, 63.7% were male with the mean age of 34.1 ± 15.43 (range [4–96 years]). About 16.6% of patients had a previous underlying disease, 34.7% had a history of psychiatric problems, and 33.0% of patients were addicted. Oral consumption (89.0%) was the most common route of poisoning. The most common poisonings were opioids/opiates, alcohols, and benzodiazepines (14.7%) in mild poisoning, multidrug poisoning (23.3%) in moderate and severe poisoning and pesticides (23%) in fatal poisoning. About11% of the patients were children <18 years old. Details of toxico-clinical characteristics and treatment modalities with respect to poisoning severity are presented in Tables 1 and 2. The fatal and severe poisoning was observed more in the male

gender both in adults ($P < 0.0001$) and children ($P = 0.04$). We analyzed different parameters between the genders. Intentional poisoning was more common in men (58.1%) compared to women (41.9%) ($P = 0.09$). Such a difference with respect to the kind of substance was detected between the two genders ($P < 0.0001$). Indeed, the most tendencies in males were indicated for opioids/opiates and pesticides (75%) and among women for psychotropic agents (84.6%). Furthermore, the mean ages of the patients in male was higher in severe and fatal poisoning compared to minor and moderate poisoning ($P = 0.01$).

The results of multivariate logistic regression to explore factors associated with the severity of poisoning are shown in Table 3. Kind of substance, level of consciousness on admission, ECG

Table 1: Comparison of toxico-demographic variables among patients with respect to poisoning severity

Variables	Poisoning severity (*n*=75)				*P*
	Minor, *n* (%)	Moderate, *n* (%)	Severe, *n* (%)	Fatal, *n* (%)	
Gender					
Male	38 (50.7)	40 (53.3)	55 (73.3)	58 (77.3)	0.000
Female	37 (49.3)	35 (46.7)	20 (26.7)	17 (22.7)	
Age, mean±SD (median; minimum-maximum)	30.19±14.28 (27; 4-70)	36.15±15.44 (32; 16-83)	32.61±13.69 (29; 12-80)	37.48±17.26 (33; 15-96)	0.01
Children	15 (45.5)	7 (21.1)	6 (18.2)	5 (15.2)	0.036
Adult	60 (22.5)	68 (25.5)	69 (25.8)	70 (26.2)	
Marriage					
Married	35 (46.6)	21 (28)	29 (38.6)	26 (34.6)	0.16
Single	40 (53.4)	54 (72)	46 (61.4)	49 (65.4)	
Addiction	19 (25.3)	28 (37.3)	29 (38.6)	21 (28)	0.27
History of the underlying somatic disease	5 (6.7)	17 (22.7)	8 (10.7)	19 (25.3)	0.002
History of psychiatry disease	20 (26.7)	33 (44)	24 (32)	25 (33.3)	0.15
Type of poisoning					
Accidental	15 (20)	5 (6.7)	3 (4.0)	4 (5.4)	0.000
Suicide	12 (16.0)	33 (44.0)	37 (49.3)	54 (72.0)	
Drug abuse	25 (33.3)	18 (24.0)	19 (25.4)	10 (13.3)	
Unknown	23 (30.7)	19 (25.3)	16 (21.3)	7 (9.3)	
Route of exposure					
Ingestion	59 (78.7)	67 (89.3)	66 (88)	74 (98.7)	0.000
Inhalation	8 (10.7)	2 (2.7)	1 (1.3)	0	
Skin contact	6 (8.0)	3 (4.0)	1 (1.3)	0	
Injection	0	0	1 (1.4)	0	
>1 route of exposure	2 (2.6)	3 (4.0)	6 (8.0)	1 (1.3)	
Kind of poisoning (substances and bites)					
Opioids/opiates	11 (14.7)	16 (21.3)	13 (17.3)	4 (5.3)	0.000
Stimulants	4 (5.3)	0	3 (4.0)	0	
Neuropsychiatric drugs	4 (5.3)	5 (6.7)	3 (4.0)	1 (1.3)	
Benzodiazepines	11 (14.7)	7 (9.3)	1 (1.3)	0	
Alcohols	11 (14.7)	2 (2.7)	6 (8.0)	8 (10.7)	
Pesticides	4 (5.3)	6 (8.0)	9 (12.0)	50 (66.7)	
Multidrugs	9 (12.0)	28 (37.3)	29 (38.8)	4 (5.3)	
NSAIDs	6 (8.0)	3 (4.0)	1 (1.3)	0	
Other medications	9 (12)	5 (6.7)	9 (12)	8 (10.7)	
Bites	6 (8.0)	3 (4.0)	1 (1.3)	0	

NSAIDs: Nonsteroid anti-inflammatory drugs, SD: Standard deviation

Table 2: Comparison of therapeutic interventions among patients with respect to poisoning severity

Therapeutic interventions	Poisoning severity (n=75)				P
	Minor, n (%)	Moderate, n (%)	Severe, n (%)	Fatal, n (%)	
Gastric lavage (prehospital)	1 (1.3)	3 (4.0)	9 (12.0)	7 (9.3)	0.02
Gastric lavage (in-hospital)	7 (9.3)	40 (53.3)	30 (40.0)	18 (24.0)	0.003
Activated charcoal (prehospital)	1 (1.3)	3 (4.0)	9 (12.0)	6 (8.0)	0.03
Activated charcoal (in-hospital)	30 (40.0)	53 (70.7)	43 (57.3)	25 (33.3)	0.000
Antidote (prehospital)	2 (2.7)	4 (5.3)	13 (17.3)	5 (6.7)	0.01
Antidote (in hospital)	14 (18.7)	43 (57.3)	40 (53.3)	17 (22.7)	0.000
Intubation (prehospital)	0	1 (1.3)	15 (20.0)	10 (13.3)	0.000
Intubation within 24 h	0	1 (1.9)	54 (72.0)	52 (69.3)	0.000
Length of hospital stay (h), mean±SD (median; minimum-maximum)	16.92±10.45 (12; 3-48)	51.20±23.11 (48; 24-168)	174.72±156.26 (120; 48-1032)	91.25±276.98 (48; 1-2376)	0.000

SD: Standard deviation

changes, administration of antidote in the prehospital setting, and time of ingestion to hospital admission were identified as independent factors associated with the severity of poisoning. One hundred and forty-nine of patients recovered without complication (49.7%). One patient in the minor poisoning group found complications. Twenty-three and 52 patients in moderate and severe poisoning groups respectively developed complications during hospitalization. Table 4 reveals the results of multivariate logistic regression to explore factors associated with outcome (complications and death). Duration of hospitalization, kind of substance, the level of consciousness, respiratory rate, and underlying disease was identified as an independent factor associated with complications and death [Table 4].

Discussion

Our study provides information on the toxico-clinical characteristics of patients based on the severity of poisoning and its relationship with outcome. The results showed the severity of poisoning (fatal) increased with age, similar to other studies in adult patients.[16,17] Although the gender and age were different among patients with poisoning severity, in the regression analysis, none of them were predictive factors. Although other studies evaluated the severity only in adults, the population of our study consisted of both children and adults. Most of the patients in our study were men and this data are in accordance with the other study that had been appraised patients in ICU admission.[18] In addition, the man-to-women ratio was increased from 1.02 in minor poisoning to 3.40 in fatal poisoning. The reason may be due to intentional and higher pesticide poisoning in men that may have high mortality. Some other studies also showed a higher mortality rate in men.[19,20] In a study related to the trend of fatal poisoning from 1990 to 2015, the fatal cases were mostly in men.[21]

In our study, similar to the other study, the majority of fatal poisoning was related to suicide attempts.[22] Overdoses had been reasons for one-fourth of all suicide attempts in

Table 3: Multivariate logistic regression analysis for prediction of variables with respect to poisoning severity

Variables	Adjusted OR* (95% CI)	P
Level of consciousness		
Lethargic	4.38 (1.84-10.42)	0.001
Obtundation/stupor/coma	195.31 (10.26-371.73)	<0.001
ECG changes (abnormal)	4.56 (1.65-12.56)	0.003
Time interval to admission in the hospital (h)	1.15 (1.02-1.28)	0.01
Antidote (prehospital)	7.08 (1.77-28.34)	0.006
Kind of substance		
Pesticides	22.12 (4.01-121.88)	0.001

*Adjusted for all variables that were significant in univariate analyses. Other variables were not significant and have not shown in the table. CI: Confidence interval, OR: Odds ratio, ECG: Electrocardiography

Table 4: Multivariate logistic regression analysis for prediction of variables related to the outcome (complications and death)

Variables	Complications and death, adjusted OR* (95% CI)	P
History of the underlying disease	3.65 (1.09-12.24)	0.03
Kind of substance		
Pesticide	13.31 (2.97-120.52)	0.02
Level of consciousness		
Obtundation/stupor/coma	66.06 (2.41-180.07)	0.01
Abnormal respiration	1.14 (1.02-1.27)	0.02
Length of hospital stay (h)	1.02 (1.01-1.03)	0.001

*Adjusted for all variables that were significant in univariate analyses. Other variables were not significant and have not shown in the table. CI: Confidence interval, OR: Odds ratio

England.[23] A history of psychiatric disorders was recorded in 34.7% of our patients. A recent epidemiological study reported 49.8% of patients had psychiatric disorders.[1] The prevalence of mental health problems, easy access to psychological prescription drugs, and low prices have made psychological drug abuse a common phenomenon in Northern Finland.[24]

We presented that the frequency of therapeutic interventions including gastric lavage, activated charcoal and antidote administration among patients with respect to poisoning severity is significantly different. Patients with severe and fatal poisoning received more than other patients. Activated charcoal is prescribed for primary elimination of the toxin in moderate to severe cases of poisoning.[25] We also observed that with increasing the need for intubation, the chance for mortality will be increased and these data are similar to other that has presented intubation on admission was highly specific at predicting mortality but not very sensitive.[26]

In our study, poisoning with multidrug, pesticides, and opiates was common in severe to fatal groups. The studies have showed different results. Ethanol or drug was the most common cause of poisoning in industrialized countries. A review study on acute poisoning in adults showed that drug combinations were the most common causes of acute poisoning.[27] Cultural differences and access to different drugs in communities can explain this difference. In fact, drug and chemical poisoning is largely influenced by socioeconomic and sociocultural factors.

The results showed that pesticide poisoning was a predictive factor of outcomes in our study. However, the large OR (13.31 [2.97–120.52]) may reduce the strength of this association in clinical practice. We did not analyze data based on the different kinds of pesticides. Aluminum phosphide, paraquat, and organophosphate poisoning are the most common pesticide intoxication in our society.[27] Since there is no definite treatment for aluminum phosphate and paraquat poisoning, the mortality is higher in these pesticides compared to other pesticides.[28] Death due to pesticide poisoning in our study was 66.7% which is higher when compared to epidemiology reported from developing countries (21% in South-East Asia).[23] However, another study[17] presented that intoxications by opiates, cocaine, and amphetamine had the highest mortality after ICU admission (12.3%). Evaluating demographic differences in suicidal behavior is imperative for the improvement of specific service provisions in the emergency department (ED).[29]

Patients with abnormal ECG changes had greater odds of severity poisoning. Although we did not categorize them based on the type of abnormality in ECG, Akdur *et al.*[30] presented that no statistically significant correlation was reported between the PSS and QTc intervals. However, Schade Hansen *et al.*[31] presented a significant rising in mortality in patients with prolonged QTc intervals. Furthermore, prolonged QTc interval was a poor indicator for prognosis in organophosphate poisoning in another study.[32] Different results were presented concerning the value of ECG, including changes in rate and rhythm for assessing poisoning severity and prognosis in cases with organophosphate poisoning.[33] Another factor which may affect the ECG is underlying diseases. There was a significant different in patients with different poisoning severity with respect to underlying diseases.

Loss of consciousness state was also the important factor that predicted both severities as well as the outcome of the poisoning. We did not determine the level of consciousness based on the Glasgow Coma Scale (GCS). However, a significant correlation has been observed between the GCS and PSS scores in another study.[30] PSS and GCS were effective tools for the designation of the severity of organophosphate poisoning[30] and other toxicities.[10] Farooqui *et al.* described a similar effect for PSS and GCS in forecasting mortality among patients with organophosphate intoxication.[34]

The time interval from poisoning to admission in the hospital was identified as another independent factor associated with the severity of poisoning as well as the outcome. Alanazi *et al.*[35] presented that among poisoned patients with delayed arrival times, more severe outcomes, particularly in the respiratory, gastrointestinal, muscular, nervous, and kidney problems, had been reported. This time is important regarding the efficiency of ED treatments, especially administering antidotes. Furthermore, a delayed arrival time over the 3 h significantly influences the length of hospital stay.[36] Delayed time is highly dependent on the issue of witnessing the occurrence of poisoning. ED admission should be performed immediately when a suspected poisoning happened.[37] Delaying in a treatment help to elevation drug initial peak serum level, consequently, leads to permanent tissue injury. Sam *et al.*[5] found a linear correlation between those two parameters as well, although they reported that clinical outcome will not influence by this duration.

In addition, in our study, underlying disease was identified as an independent factor associated with complications and death. The previous study has been demonstrated that history of disease could predict the outcomes of hospitalized patients with acute poisoning.[11,38]

Finally, patients with severe poisoning received antidote 7.08 times more compared to others. The previous study has been shown that prehospital treatment of poisonings will be causes with short-term mortality.[39]

CONCLUSIONS

The loss of consciousness, prehospital antidote administration, abnormal ECG, underlying disease, abnormal respiration, delay to presentation to hospital, and longer length of hospital stay can be considered important factors for determining poisoning severity and outcome. It is suggested to include all these significant variables in scoring systems for better outcomes evaluation and do anterograde researches. Medical toxicologists can consider these predictive variables when triage the patients for hospitalization in the ICU. The burdens of poisonings as a public health problem need for better investigation and understanding of this topic. This study highlights the need to develop a toxico-vigilance system in our society.

Limitations of the study

The study was cross-sectional and both adults and children were evaluated in this study. As the outcome and severity of poisoning can be different in these two age groups, a new research specifically in children is suggested. Furthrore, the number of patients in some poisoning such as pesticides poisoning was low. Therefore, although the results showed that the OR in pesticide poisoning with respect to severity and outcome was significant, the large OR needs research on more patients to be able to validate this issue.

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Conflicts of interest

There are no conflicts of interest.

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