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ORIGINAL ARTICLE

A 3-Year Survey of Mushroom-Poisoned Patients: Clinical Features, Management and Outcomes

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Abstract

Background: Besides their nutritional value, mushrooms have shown beneficial effects on human body organs; thus, people are interested in consumption of mushrooms regardless of their safety. In this report, we present patients with suspected mushroom poisoning, who were admitted to the Medical Toxicology Department of Imam Reza Hospital, Mashhad University of Medical Sciences, Mashhad, Iran.
Method: Seventeen mushroom-poisoned patients were admitted to our department from April 2012 to May 2015. Following the evaluation of the vital signs, biochemical analysis was done and in parallel, treatment was initiated based on the laboratory tests results and clinical manifestations.
Results: In this period, 17 mushroom-poisoned individuals (11 males (64.7%) and 6 females (35.3%) with mean age of 28.26±18.05 years old) were referred to our department. Subjects presenting the signs of intoxication within 6 hours post-ingestion comprised 58.8% of our patients. The rate of mortality was zero but 3 patients presented with some levels of unconsciousness. Only one patient had augmented levels of AST with no evidence of hepatic failure. Coagulopathy as reflected by increased INR was observed in 2 patients. Regarding the season in which the poisoning occurred, the majority of cases happened in spring and autumn.
Conclusion: Similar to other reports on mushroom-poisoned patients, we observed gastrointestinal disturbances as the major symptom. Since the majority of mushroom poisoning cases occur following the ingestion of accidentally picked mushrooms, risk communication practices should be improved to increase the public awareness of mushrooms toxic effects.

Keywords: Amatoxin; Epidemiology; Mushroom poisoning; Survey

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INTRODUCTION

During the past decades, people have increasingly become interested in mushrooms as they possess a unique taste and are rich in proteins. Also, considerable scientific evidence supports their beneficial effects on human systems (1-3). Therefore, the number of individuals seeking wild consumable mushrooms has expanded resulting in enhanced risk of mushroom-induced poisoning (4). It should be noted that even edible mushrooms can induce toxicity if the collection, storage, transportation or cooking is not done appropriately (5). Interestingly, between 2000 and 1.5 million mushroom species are found in Europe, among which approximately 100 species are considered poisonous (5-7). In Europe, ingestion of wild mushrooms accounts for around 5 in 100,000 cases of poisoning, suggesting mushrooms as a rare cause of intoxication (6).

Manifestations of mushrooms intoxication may vary based on the species of the consumed mushroom (7-9). However, different species may induce common clinical symptoms such as gastrointestinal disturbances, which are the most frequently seen manifestations (8,9). It has been reported that subjects who present with intoxication manifestations during 6 hours after mushroom ingestion, are classified as mild cases that generally need symptomatic management. For instance, it was reported that administration of intravenous fluids to most of patients with mild intoxication is an adequate treatment approach (10). On the other hand, if symptoms appear after a 6-hour lag post-ingestion, an augmented risk of hepatic or renal failure, intravascular hemolysis, rhabdomyolysis, or disturbances in electrolytes is anticipated; however, it cannot be considered a precise predictor (3, 8, 11, 12).

Manifestations of mushroom poisoning markedly differ based on the type of the consumed mushroom. For example, it is commonly accepted that treatment of amatoxine poisoning requires a more serious approach, including fluid replacement, rectification of electrolytes imbalance and coagulopathy, and oral administration of charcoal (12-14).

Since the exact type of the digested mushroom is often unclear even to the patient, management of mushroom poisoning is a challenging issue (4,8,9). Moreover, initial

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manifestations of mushroom poisoning are not reliable predictors of serious outcomes that may appear later (15).

In this report, we present demographic information, clinical manifestations, and the rate of mortality of mushroom-poisoned patients who were admitted to the Medical Toxicology Department of Imam Reza Hospital, Mashhad, Iran from April 2012 to May 2015.

METHODS

In this study, we performed a retrospective single-center evaluation of medical records of individuals who were admitted to the Medical Toxicology Department of Imam Reza Hospital, Mashhad, Khorasan Razavi Province, northeastern Iran from April 2012 to May 2015 and diagnosed with mushroom poisoning. All cases of poisoning in Khorasan Razavi Province are referred to this academic center. This study was approved by the Ethics Committee of Mashhad University of Medical Sciences, Mashhad, Iran.

Data collection

Demographic information, clinical manifestations, biochemical analysis data (levels of liver enzymes, bilirubin, coagulation profile, etc.) and mortality among mushroom-poisoned patients were recorded. Generally, patients were divided into "early" who presented the intoxication manifestations within 6 hours after mushroom intake, and "late" referring to those who showed signs of poisoning later than 6 hours post-intake. Also, therapeutic approaches used for management of the patients are mentioned.

Statistical analysis

For data analysis, SPSS software program version 23.0 (SPSS Inc., Chicago, IL, USA) was used. Data normality was verified using the Kolmogorov-Smirnov test. Data are presented as either mean±SD or number (percentage). Student t-test or Mann-Whitney U test was used to test for significant differences, where appropriate. Fisher's exact test was used for qualitative variables. $p<0.05$ was considered statistically significant.

RESULTS

From April 2012 to May 2015, 17 patients (11 males and 6 females comprising 64.7 and 35.3 % of the patients, respectively) with the mean age of 28.26±18.05 (ranging from 4 to 54 years old) were diagnosed with mushroom poisoning at the time of admission to our center. Vital signs of mushroom-intoxicated patients at the time of hospital admission are noted in Table 1. According to our data, 58.8% of the patients presented manifestations of mushroom intoxication, 6 hours after mushroom intake. Among our patients, a mortality rate of zero was observed while 3 patients (17.6%) presented different levels of unconsciousness. The mean±SD of vital signs observed in mushroom-poisoned patients is mentioned in Figure 1.

The laboratory test results on blood samples taken from the subjects are shown in Table 2. Concerning biochemical parameters, 1 patient presented elevated levels (>400 U/L) of AST. Though augmented levels of aminotransferases were recorded, no patients showed signs of hepatic failure. Based on creatinine and BUN levels, none of the patients had developed renal dysfunction. Increased INR was seen in 2 patients, reflecting the occurrence of coagulopathy.

It should be noted that 76.5% of poisonings occurred due to accidental picking of mushrooms grown in rural areas and 4 (23.5%) patients were poisoned following the consumption of labeled packed products sold in markets. Moreover, 14 (82.4%) of poisonings cases occurred in spring and autumn (Figure 2).

Regarding clinical manifestations, no statistically significant differences were observed between early and late groups ($p>0.05$). Also, the two groups of patients did not significantly differ in terms of level of consciousness and

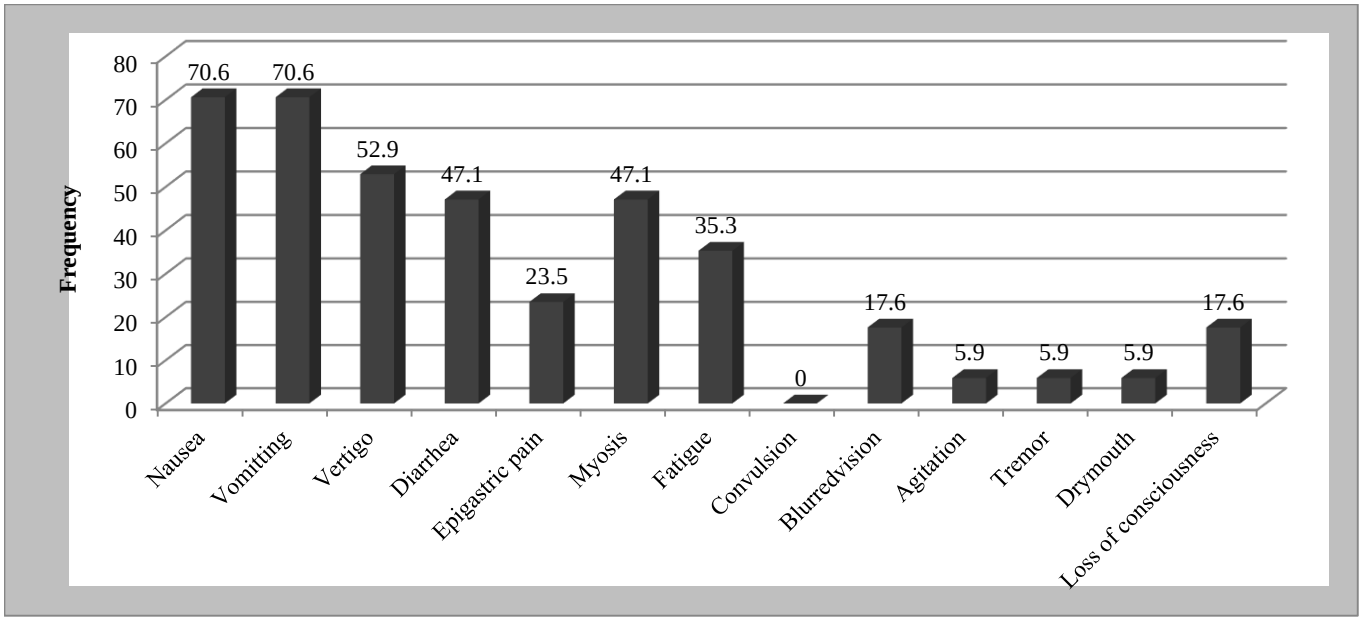

Figure 1. The frequency of clinical symptoms observed in mushroom-intoxicated patients admitted to our center from April 2012 to May 2015.

Table1. Vital signs of mushroom-intoxicated patients at the time of hospital admission.

Vital sign	Mean±SD	Range
Systolic BP	107.88 ± 18.25 mmHg	80-130 mmHg
Diastolic BP	69.76 ± 16.25 mmHg	40-100 mmHg
Pulse rate	94.65 ± 14.39 beats/min	68-120 beats/min

Table 2. Results of biochemical analysis of blood samples.

Biochemical marker	Frequency	Percentage	Biochemical marker	Frequency	Percentage
Hyponatremia	2	11.8	AST (U/L), 40-100	16	94.2
Hypernatremia	-	-	AST (U/L), 100-400	-	-
Hypokalemia	2	11.8	AST (U/L), >400	1	5.8
Hyperkalemia	1	5.8	ALT (U/L), 40-100	16	94.2
Creatinine(mg/dl),<1	6	35.2	ALT (U/L), 100-400	-	-
Creatinine(mg/dl),1-3	11	64.7	ALT (U/L), >400	1	5.8
Creatinine(mg/dl),>3	-	-	PT (s), >14	4	23.5
BUN (mg/dl), (40–100)	-	-	PTT (s), >35	3	17.6
Hyperglycemia (> 200 mg/dl)	3	17.6	INR > 1.1	2	11.8
Bilirubin Total (mg/dl), (> 1)*	3	30	Elevated WBC, (>12000 U/L)	3	17.6
			Thrombocytopenia, (<100000 U/L)	1	5.8

*The level of total Bilirubin was available and included in this Table, for 10 patients only. BUN: Blood Urea Nitrogen; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; PT: Prothrombin Time; PTT: activated partial thromboplastin time; INR: International Normalized Ratio; and WBC: White Blood Cell.

levels of Na, K, Cr, Plt, blood pressure (BP), pulse rate (PR), urea, WBC, AST, ALT, blood sugar (BS) and diastolic blood pressure ($p>0.05$). It should be noted that blurred vision was more frequently seen in the early group as compared to the late group ($p=0.036$) (data not shown).

Therapeutic measures

In our study, penicillin and NAC were given for management of mushroom-poisoning to 58.8% and 35.3% of patients, respectively. Gastric lavage was done for 7 (41%) patients. Moreover, 1 patient received vitamin K. Also, ondansetron, vitamin B6, sodium bicarbonate, and potassium chloride were administered as needed.

Following intoxication, based on the type of the consumed mushrooms and the toxin content, clinical manifestations may include gastroenteritis and CNS conditions (both considered as transient outcomes) as well as hepatic failure (which may become irreversible and require liver transplantation) (16-18). Also, the mushrooms *Amanita smithiana* and *Amanita proxima* have been reported to be nephrotoxic as they induce

DISCUSSION

Mushroom poisoning is generally regarded as an accidental intoxication and using mushrooms for committing suicide or homicide hardly occurs. Annually, almost 50-100 deaths per year occur due to mushroom poisoning (16). In Turkey, the majority of plant-induced intoxications are attributed to mushroom poisoning (11). gastrointestinal disturbances followed by severe hepatic and renal failure (19). Ingestion of amatoxin-containing mushrooms accounts for 90-95% of mushroom-poisoning deaths. Alpha-amanitin, as the main amatoxin, as well as beta-amanitin are assumed to be the cause of mushroom intoxications (11). Amatoxins are not destroyed by cooking or even following prolonged storage at cold temperatures (20). Even 0.1 mg/kg body weight of amatoxins could be sufficient to induce death in adults (11). Following ingestions, hepatocytes uptake significant amounts of amatoxin, resulting in hepatocytes damage causing increased levels of AST and ALT in serum in *Amanita* species-induced poisonings (21). It was shown that augmented levels of AST and ALT may cause hepatic coma, reflecting a marked relation between the enzymes levels and fatality (4).

Several reports have shown that the lag time between the ingestion of mushroom and onset of symptoms is a reliable predictor of the severity of consequences (22). In this regard, patients with late onset toxicities(presenting symptoms later than 6 hours post mushroom consumption), may experience renal and/or hepatic failure, which are serious conditions that may lead to death (10).

As shown in Figure 2, mushroom poisoning in Khorasan

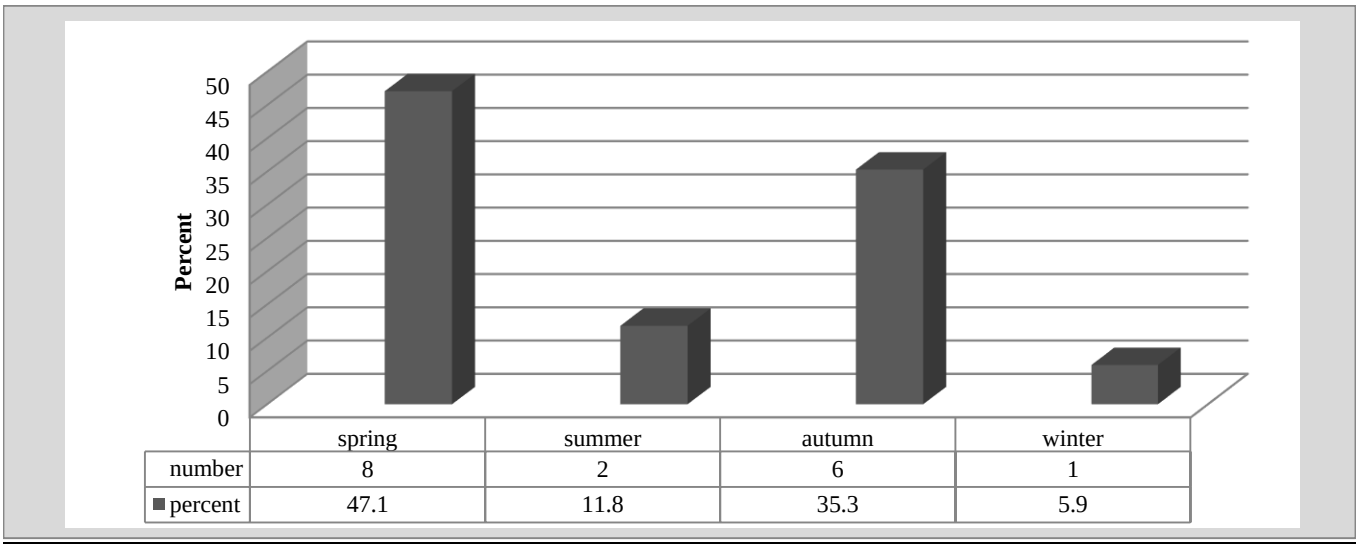

Figure 2. The frequency of mushroom poisoning in different seasons from April 2012 to May 2015.

Razavi Province, northeastern Iran peaks in spring and autumn, which was consistent with the report of Cevik and Unluoglu (23). However, Schenk-Jaeger et al. and Ishihara and Yamuara reported that the highest rate of mushroom poisoning is observed in late summer (6, 14).

It was reported that decreased sodium levels and increased urea, AST, ALT, total bilirubin lactate dehydrogenase, prothrombin time, international normalized ratio (INR) and activated partial thromboplastin are linked with augmented risk of death (24). Nonetheless, in our study, slight increases in ALT, AST and INR reflected liver damages which did not lead to hepatic failure. Also, the rates of renal failure and mortality were zero. It should be also noted that, in our previous report, the prevalence of mushroom poisoning among individuals admitted to our center was 0.1% while a marked rate of mortality (22%) was observed (25).

Based on the type and amount of the mushroom consumed, mushroom intoxication may result in different forms of gastrointestinal (i.e., nausea, vomiting and diarrhea), neurologic, hepatic and renal complications (23).

American Association of Poison Control Centers (AAPCC) has declared that the type of the ingested mushroom was unknown in 79.3% of cases in 2010 (26). Consistently, the limitation of our study results is that since the type of the mushroom causing intoxication was not known, it is difficult to discuss the relation between the mushroom and/or mushroom toxins type with the clinical symptoms and their severity and draw definite conclusions. However, as our center is the principal poisoning center of northeastern Iran, all poisoned patients living in this region refer to this center. According to the literature, the lag time between the mushroom ingestion and onset of poisoning symptoms could be regarded as the most important factor determining the required management of mushroom-poisoned patients as well as their fate; however, in this study, there was no difference in outcomes between the early and late groups, which could be possibly due to the quality of care and treatment offered in this department.

CONCLUSION

As the majority of mushroom poisoning cases occur following the ingestion of accidentally picked mushrooms, risk communication practices should be improved to increase the public awareness of mushrooms toxic effects.

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Of the present study show that BUP is superior

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