Clinical Profile and Outcome of Patients Presenting with Mushroom Poisoning in a Tertiary Care Center of Eastern Nepal

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ABSTRACT

Introduction: Accidental mushroom poisoning is constantly seen and regularly reported from all over world. Exact magnitude of problem and its clinical profile in Nepal is not well known. This study was done to evaluate clinical profile and treatment outcome of patients presenting with mushroom poisoning in the department of internal medicine, BPKIHS, Dharan.

Methods: It is a prospective observational study conducted in department of internal medicine, BPKIHS, Dharan from 1st January 2008 to 31st December 2009. Informed consent was taken. All the patients were subjected to necessary laboratory investigation. They were followed up at 1 week and 1 month after discharge.

Results: All together 60 patients were analyzed. Majority of subjects 56 (93.3%) were from rural areas. Vomiting and diarrhea were the two most common presentations seen in 56 (93.3%) subjects. The latent period for the symptoms were >6 hours in 4 (6.7%) and <6 hours in 56 (93.3%) subjects. Fulminant hepatic failure was seen in 6 (10%) subjects and among them 4 (66.7%) expired. After admission 3 (5%) subjects developed GI bleeding. Average duration of hospital stay was 4.6 days. In follow up recovery was complete in all subjects who survived the acute phase of poisoning.

Conclusions: Especially in patients coming during rainy season mushroom poisoning should be considered in the differential diagnosis of acute gastroenteritis. Mortality is high in subjects with FHF whereas recovery is complete in subjects who survived the acute phase.

Keywords: *fulminant hepatic failure; gastroenteritis; mushroom poisoning; wild mushrooms.*

INTRODUCTION

Mushroom poisoning refers to deleterious effects resulting from ingestion of toxic substances present in a mushroom. Although over 5000 varieties of mushrooms are present in the world, but only a 100 are toxic.[1] Utility values of Nepalese mushrooms has been tabulated by Adhikari are 110 as edible, 13 as medicinal, 45 as toxic and 6 others.[2] Accidental mushroom poisoning is constantly seen all over world. Personalities like Claudius and Pope Clement VII are said to have been murdered by mushroom poisoning.[3]

According to mushroom poisoning registry of the North American Mycological Association incidence is 5/100,000 population per year.[4] Though many fatal

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cases are reported the exact magnitude of problem and it's clinical profile in Nepal is not well known.[5] In Nepal, the mortality had been found to occur around 15-20 annually.[6]

This study was carried out to evaluate clinical profile and treatment outcome of patients presenting with mushroom poisoning.

METHODS

It is a prospective observational study conducted in the department of internal medicine, BP Koirala Institute of Health Sciences, Dharan, Nepal which is a tertiary care center located in eastern part of Nepal. All the suspected patients of mushroom poisoning presented in the department of internal medicine from 1st January 2008 to 31st December 2009 were included in the study. Mushroom poisoning was diagnosed clinically and historically in patients who had history of eating mushrooms preceding the illness. Written informed consent was taken from all the patients. The study was cleared by ethical and institutional review committee. Detailed history and physical examination was carried out in all the subjects and data was collected as per predesigned proforma. All the patients were subjected to laboratory investigations like haemoglobin, renal function tests, liver function tests, prothrombin time, serum electrolytes, random blood sugar, urine for routine and microscopic examination, ECG, HBsAg and Anti HCV. Subjects were managed in standard way with fluid resuscitation and maintenance of proper hydration. Gastric lavage was done in those who arrived within six hours of ingestion. Serial Prothrombin time and LFT were done and other tests were repeated as when required. Vitamin K was give to all patients who have increased in prothrombin time. In those patients where Amanita Phalloides poisoning was suspected, Crystalline Penicillin and sylimarin was also prescribed. All the patients were admitted in the hospital till symptoms subside and abnormal blood parameters come to normal. All the patients who survived were discharged and further followed up at one week and one month. The collected data were entered into Microsoft Excel Spreadsheet and analyzed using SPSS ver 11.5 (PC) / Epilnfo (CDC, Atlanta, GA, USA). Means and standard deviation was calculated.

RESULTS

All together 60 patients came with mushroom poisoning during the study period were enrolled and analysed. Mean age of our patients was 33.1 ± 18.1 years (ranging from 14-75 years). There were 26 (43.33%) male and 34 (56.67%) were female. The baseline demographic data is shown in (Table 1).

Table 1. Baseline characteristics of patients with mushroom poisoning.

Age (yrs) Mean ± SD	33.1 ± 18.1
Female sex no (%)	34 (56.7)
Rural no (%)	56 (93.3)
Urban no (%)	04 (6.7)
Source of Mushroom	
Forest no (%)	49 (86.66%)
Garden no (%)	10 (16.67%)
Market no (%)	1 (1.67%)
Duration from ingestion to first symptom	
>6 hours no (%)	4 (6.67%)
<6 hours no (%)	56 (93.33%)
Time to reach the hospital (hrs) Mean ± SD	11.38 ± 5.61
Clinical symptoms	
Vomitting no (%)	56 (93.33%)
Diarrhoea no (%)	27 (45%)
Altered Sensorium no (%)	6 (10%)
Hallucination no (%)	2 (3.33%)
Anticholinergic symptoms no (%)	2 (3.33%)
Pulse (Beats/min) Mean ± SD	85.4 ± 9.14
SBP (mmHg) Mean ± SD	121 ± 15.74
DBP (mmHg) Mean ± SD	77.8 ± 11.61
Haemoglobin (g/dl) Mean ± SD	12.8 ± 2.25
TLC (/cu.mm) Mean ± SD	11986 ± 3477
Platelets (/Cu.mm) Mean ± SD	258217 ± 125054
RBS (gm/dl) Mean ± SD	100 ± 30.34
INR Mean ± SD	1.84 ± 1.59
Serum Urea (mg/dl) Mean ± SD	28.83 ± 8.94
Serum Creatinine(mg/dl) Mean ± SD	0.96 ± 0.50
Total Protein(mg/dl) Mean ± SD	6.89 ± 0.69
Albumin(mg/dl) Mean ± SD	4.38 ± 0.49
Total Bilirubin(mg/dl) Mean ± SD	1.23 ± 1.73
AST (IU/L) Mean ± SD	65 ± 135.07
ALT (IU/L) Mean ± SD	72.1 ± 159.27
Alkaline phosphatase(IU/L)	206.52 ± 129.67
Duration of hospital Stay (days)	4.57 ± 1.69

There were patients from eight nearby districts. Maximum number of patients 30 (50%) were from Morang district followed by 9 (15%) from Jhapa, 7 (11.67%) from Sunsari, 4 (6.67%) from Ilam, 3 (5%) from Panchthar, 3 (5%) from Udaypur and 2 (3.33%) each from Terhathum and Dhankutta district (Figure 1).

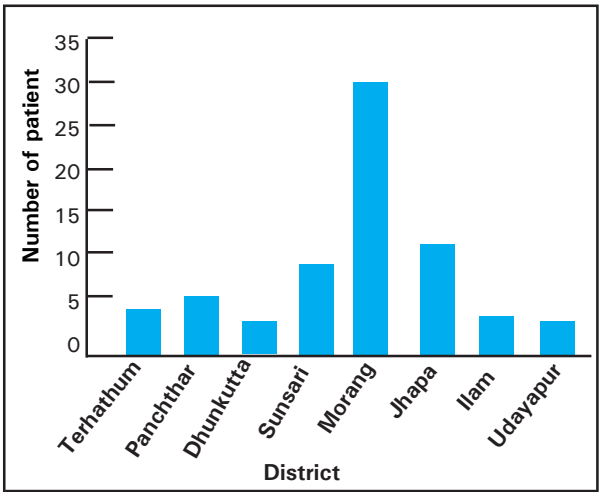

Figure 1. Geographical distribution of patients presenting with mushroom poisoining.

Ethnically mushroom poisoning was more common in people of Mongolian descents [38 (63.33%)] like Rai 13 (21.67%), Magar 11 (18.33%), Gurung 5 (8.33), Tamang 3 (5%), Sherpa 3 (5%), Limbu 2 (3.33%) and Lama 1 (1.67%). Other ethnic groups were Dhimal 8 (13.33%) Newar 5 (8.33%), Uraw 3 (5%), Brahmins 3 (5%), Kshetriya 2 (3.33%) and Bishwakarma 1 (1.67%). Our patients came in rainy season between May to October with peak incidence in June and September (Figure 2).

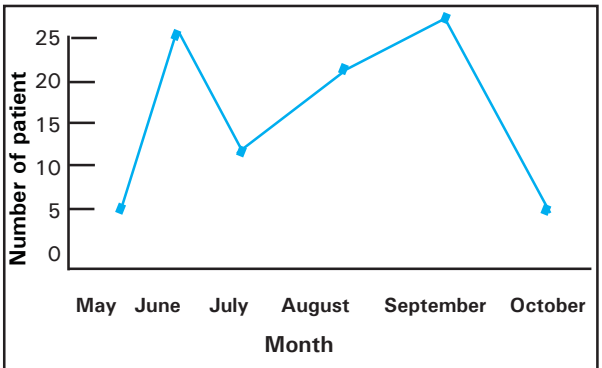

Figure 2. Monthly distribution of mushroom poisoining.

Thirty (50%) person with mushroom poisoning in our series did not receive any formal education. Majority of our patients 56 (93.33%) were from rural areas whereas only four (6.67%) were from urban areas. Average time required to arrive our hospital was 11.38±5.61 hrs (4 hrs -5 days). Awareness regarding poisonous mushroom was present in majority of patients. Fifty two patients (86.67%) subjects knew that poisoning can occur after consuming mushrooms. On asking about reasons of eating mushroom, 56 (93.33%) said that they like the taste of mushroom and rest 4 (6.67%) said that they ate it to save some money. All our patients had accidental mushroom poisoning. Fifty nine patients (98.33%) developed poisoning after ingestion of wild mushrooms collected from the forest 49 (86.67%) or from the backyards 10 (16.67%). There was one incidence of mushroom poisoning from commercially cultivated mushroom which this person had bought from the market.

Gastrointestinal symptoms like nausea, vomiting and diarrhoea were the most commonly encountered symptoms, other presenting symptoms were altered sensorium, dry mouth. Vomiting was present in 56 (93.33%) subjects and diarrhoea was present in 27 (45%) subjects. Nine (15%) subjects were having altered sensorium and two (3.33%) were having dry mouth and dizziness. The latent period for the symptoms were >6 hours in four (6.67%) and <6 hours in 56 (93.33%) subjects. Most common complication seen in our patients were Fulminant hepatic failure which was developed in six (10%) subjects and among them four (66.7%) expired. After admission 3 (5%) subjects developed GI bleeding. Average duration of hospital stay was 4.6 days (1-9 days). In follow up recovery was complete in all subjects who survived the acute phase of poisoning.

DISCUSSION

There are many cases of mushroom poisoning which occur in Nepal annually, mostly due to misidentification of edible mushrooms especially during rainy monsoon season. Here we have presented the first prospective study of mushroom poisoning in eastern region of Nepal in medical literature. The popular interest in gathering and eating uncultivated mushrooms has been associated with an increase in incidents of serious mushroom-related poisonings.[7] In large amount mushrooms grow and flourish in wild during the fall or rainy season. The mature cap usually is metallic green but varies from light yellow to greenish-brown. Amanita Phalloides, like most mushroom species, is not unique in appearance and can be mistaken for non-poisonous species. It has no distinct taste or smell. The poisonous mushrooms cannot be detoxified by cooking, freezing, drying or by any other means. People mainly from rural areas forge mushroom as it is a good quality delicious food available free of cost during rainy season. People mainly villagers with a very little education and knowledge misidentify poisonous mushroom with edible mushroom. In Nepal

various mycophagous groups such as Sherpa, Tamang, Gurung, Magar, Tharu, Danuwar, Newar, Kami, Damai, and Sarki are directly concerned with the collection and consumption of mushrooms. It is generally believed that Brahmins do not use mushrooms. However, nowadays Brahmins have also started to cultivate and use various mushrooms.[8] Majority of mushroom poisonings in children especially in the "grazing" stage are due to ingestion of mushrooms found in the lawn while playing. A few poisonings are the result of misidentification while attempting to collect hallucinogenic mushrooms for recreational use.[9] The symptomatology varies with individual susceptibility, even within the same individual on different occasions, in addition to other factors i.e., amount, variety, age, geographical location and premorbid hepatic and renal conditions. The majority of toxic mushrooms cause early onset, self-limiting gastroenteritis due to wide variety of gastrointestinal irritants. The symptoms usually appear within 20 minutes to 4 hours of ingesting the mushrooms. It includes nausea, vomiting, cramps and diarrhoea, which normally subside after the irritant had been expelled. Severe cases may require hospitalization. Treatment is largely supportive - helping the patient's body to eliminate what it's not equipped to handle. Recovery is usually complete. Every physician should consider mushroom poisoning in the differential diagnosis of acute gastroenteritis and renal failure, especially in high prevalent regions. Fatality in mushroom poisoning is usually resulted from late onset, amanitin or gyromitrin type protoplasmic toxins.[10] Ingestion of Amanita Phalloides may account for approximately 90% of deaths attributable to mushroom ingestion worldwide.[7,11,12] If the gastrointestinal distress begins 6 to 24 hours after ingestion of the mushrooms, there is a possibility of a very serious toxicity from Amanita Phalloides. Gastrointestinal symptoms of 4-11 hours onset with impaired kidney function could be due to Allenic Norleucine (2-amino-4,5-hexadienoic acid). The gastrointestinal symptoms of onset greater that 24 hours and up to 21 days can be due to Orellanine. Amanita muscaria produces a toxic alkaloid, ibotenic acid, which has a rapid onset muscarinic effect (dizziness, muscular jerking, staggering, confusion and coma) while Amanita Phalloides produces a thermostable nitrogenous cyclic octapeptide, amanitine or amatoxin (alpha and beta) which selectively inhibits the nuclear RNA polymerase II, resulting in hepatic and renal cellular derangement. Besides producing thermolabile hemolytic glycoside, amanita hemolysin, another putative toxin, phalloidin, also causes hepatocellular damage. The median lethal dose for amatoxin is 0.1 mg to 0.3 mg of the toxin per kg of body weight.[7,13] In amanita poisoning, symptoms typically occur in a progression through three stages. During the first stage, which occurs 6-24 hours after ingestion, symptoms may include severe gastrointestinal manifestatons like severe diarrhea, nausea, vomiting, abdominal pain, fever, tachycardia, hyperglycemia, hypotension, and electrolyte imbalance. During the second stage, which occurs during the next 24-48 hours, abdominal symptoms appear to abate even as hepatic and renal functions deteriorate. During the third stage, which occurs 3-5 days after the ingestion, hepatocellular damage and renal failure may progress, resulting in coagulopathy (epistaxis, hematuria, melena and hematemesis), encephalopathy (muscular twitching, excitement, delirium, coma, convulsion) or rarely cardiomyopathy.[7,13,14] Death from Amanita Phalloides poisoning may occur 4-9 days after ingestion. Fatal outcomes are associated with age less than 10 years, a short latency between ingestion and onset of symptoms, and severe coagulopathy. The fatality rate among persons treated for A. phalloides poisoning is 20%-30%.[7,12] Amatoxin can be detected by high performance liquid chromatography (HPLC) or radioimmunoassay (RIA) from plasma, feces, urine or vomitus of the patients.[7,11] Species-specific identification of the major cooked and fresh poisonous mushrooms in Japan have been possible by using a real-time PCR system. With this species-specific identification of poisonous mushrooms are now possible within 1.5 hours.[15]

Amanita Phalloides poisoning has no specific antidote. The main treatment is vigorous intravenous fluid replacement and correction of electrolyte disturbances,[7,13] correction of coagulopathy, if present. Physicians should perform gastric lavage and administer repeated doses of activated charcoal to remove any unabsorbed Amanita and to interrupt the enterohepatic circulation of the toxin.[11,13] Although some therapeutic regimens have included the administration of penicillin, cimetidine, silibinin, thioctic acid or N-acetylcysteine, these treatments have not been confirmed by clinical trials to be effective. They are not found to be effective in murine model.[16] Benzyl penicillin displaces amatoxin from plasma protein binding site, increase renal excretion and inhibit hepatocyte penetration. Silymarin is a potent antioxidant and is known to prevent hepatocyte membrane lipid peroxidation, free radical damage and blockage of α-amatoxin uptake.[13] Hemodialysis and hemoperfusion may be effective in removing the toxin if initiated within 24 hours of ingestion.[17] The only definitive treatment may be liver transplantation once fulminant liver failure occurs.[11,12] In Europe, early hospitalization, rapid diagnosis and aggressive management with charcoal hemoperfusion, thioctic acid, plasma exchange, extracorporeal liver assist device (ELAD) or orthotopic liver transplantation have shown to reduce mortality to 10% whereas 60-hour delay increases it to 50–90%.[18]

The essential steps of management would be early hospitalization, charcoal gastric lavage conventional fluid, dextrose, penicillin and silymarin therapy with hepatorenal support. Unintentional ingestion of Amanita Phalloides can be prevented by raising public awareness about wild mushroom poisoning. It can be carried out with field based proper public education programme. Education campaigns should be established in areas where Amanita Phalloides is common to educate the public about the potentially lethal consequences associated with eating uncultivated mushrooms. Use of mass media can be very helpful. It must be stressed that no wild mushrooms should be eaten unless identified as non-poisonous by a competent mycologist. Identifying mushrooms is an exact art that is very difficult and time-consuming. Mushrooms are described by size, color, color changes, texture, order, taste, gap, gills, stem/stipe, veil, annulus, volva, mycelium, and spore prints. Before making a positive identification, mycologists look closely at the color, gills, spores, stalks and base portion of the mushroom. Spores are examined under a microscope to detect differences. The mycologist will also consider where the mushroom was growing, such as in the woods, on a lawn or on a tree before making an identification. Individual spores are too small to be seen with the naked eye, but you can make a spore print that will show the color of the spores in mass. This color is an important identifying characteristic for many mushrooms, especially the gilled fungi. To make a spore print, cut the stem off the mushroom and place the cap gill-side or pore-side down on a piece of white paper. To best see the spore color, use on sheet of black paper and one of white, taped together side-by-side. Cover with a bowl or jar. If the mushroom is at the right stage-not too young, too old or deteriorated-the spores will slowly collect on the paper. A spore print will be visible in one to 12 hours.

Field guides do not provide sufficient details to differentiate toxic from nontoxic species. Poison-control centers must be established to reduce the mortality. These centers can provide expertise in identifying the toxic mushrooms, clinically managing the mushroom poisoning and can impart public education.

CONCLUSIONS

Especially in patients coming from rural areas during rainy season, mushroom poisoning should be considered in the differential diagnosis of acute gastroenteritis. Mortality is high in subjects with fulminant hepatic failure whereas recovery is complete in subjects who survived the acute phase.

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