

INTRODUCTION

Mushroom poisoning among other forms of poisoning contributes to high morbidity and mortality in the country. In certain ethnic populations of India, mushroom is an important constituent of their diet. The incidence of mushroom poisoning in India in the recent years has been recognized due to increasing awareness and the affected individuals seeking health care at the earliest. The tropical belt of the country with its biodiversity is a mother load of different fungal mushroom species. As per studies conducted in India, there are 1200 species with only 50 to 100 species known to be poisonous. Twelve groups of the identified mushroom toxins have been identified responsible for 14 described clinical syndromes.

EPIDEMIOLOGY

From the studies conducted the 50-100 toxic mushrooms produces the mycotoxins responsible for different clinical syndromes which are described below. In the United States the North American mycological association maintains a case registry where instances of mushroom poisoning are being reported. In India mushroom forms part of the diet especially in the ethnic populations. In most of the cases mushroom poisoning occurs from consumption of the wild mushrooms. However most of the cases are undiagnosed, unreported and epidemics of mushroom poisoning are reported in press which has been observed mostly in the monsoon season. Table 1 shows the different mushroom species with their toxins and mortality percentage.

From the case reports in India the reported cases are from the tribal areas of South India, the Eastern Ghats, Northern India and north eastern parts of the country. Most of the cases are being reported and documented in newspapers where mortality of such cases are being noticed. As per the clinical syndromes of most of the fatalities, they are very suggestive of *Amanita phalloides* poisoning (Table 2).

CLINICAL SYNDROMES

The 14 types of clinical syndromes caused by the 12 groups are described below. The syndromes are divided on the basis of their presentation as early onset (< 6 hours of ingestion) and late onset (> 6 hours of ingestion). The syndromic presentation and their identification help in making early diagnosis and empirical therapy.

Early onset syndromes are less toxic and life threatening, however does not exclude the possibility of consumption of lethal mushrooms.

Acute gastroenteritis – A wide variety of non eatable mushrooms when consumed causes nausea, vomiting, diarrhea and abdominal cramps within one to three hours of consumption. These symptoms are caused most commonly by the chlorophyllum molybdites species are also called “backyard mushrooms”.

NEUROTOXIC SYNDROMES

- a. The hallucinogenic effects are produced by the ingestion of mushroom containing psilocybin and psilocin. They are known to be abused for recreational purposes.
- b. CNS excitation and depression: This syndrome is caused by *Amanita* species containing toxins muscimol and ibotenic acid. Muscimol is a CNS depressant whereas ibotenic acid has excitatory effects at glutamic acid receptors in the CNS. Symptoms include somnolence, dizziness, hallucination, dysphoria, bizarre behavior and seizures.
- c. Cholinergic poisoning occurs when there is intake of *Inocybe* and *Clitocybe* species which contain muscarine toxin. Muscarine is structurally similar to acetylcholine and causes toxicity by binding to postganglionic cholinergic neurons in the autonomic nervous system. Symptoms usually appear 30 minutes post ingestion in the form of bradycardia, diaphoresis, salivation, lacrimation, bronchospasm, bronchorrhoea and incontinence.

Disulfiram like reaction: The toxin coprine found in the *Coprinus atramentarius*, the inky cap mushroom and its species are known to cause this syndrome. The symptoms occur after 2 hours of ingestion in the form of headache, flushing of face, neck and trunk, nausea and vomiting, tachycardia, palpitations, chest pain, dyspnoea.

Delayed onset syndrome (>6 hours) occurs mostly after ingestion of lethal mushrooms.

Gastroenteritis and delayed renal failure are encountered with the *Amanita* species particularly *Amanita smithiana*. Onset of renal failure is observed 12-24 hours after ingestion. General supportive care is the management of choice with few patients requiring hemodialysis.

Delayed gastroenteritis and liver toxicity : Delayed onset of vomiting, diarrhoea, and hepatitis observed more than 6 hours post ingestion are known to be life threatening complications mostly observed with toxic mushrooms, *Amanita*, *Galerina* and *Lepiota* of which the *Amanita*

Table 1: Different types of mycotoxins

Mycotoxins	Mushroom species	Mortality
Cyclopeptides : Amatoxins, Phallotoxins	Amanita phalloides A.virosa A.verna A.bisporigera Galerina marginata G.venenata Lepiota helveola	2-30 percent
Gyromitrin	Gyromitra esculenta G.infula Sarcosphaera coronaria Cyathipodia macropus	0-10%
Orellanine, orelline, cortinarin	Cortinarius orellanus C.speciosissinus Mycena pura Omphalatus olearius	End stage renal failure 11% Renal transplant 13 %
Allenic norleucine	Amanita smithiana	Full recovery
Coprine	Coprinus atramentarius Clitocybe clavipes	Full recovery
Muscarine	Citocybe dealbata C.illudens Inocybe fastigiata Boletus calopus	Full recovery
Ibotenic acid, muscimol	Amanita muscaria A.pantherina A.gemmata	Full recovery
Psilocybin , psilocin	Psilocybe cubensis P.mexicana Conocybe cyanopus Gymnopilus aeruginosa	Full recovery
GI irritants	Chlorophyllum molybdites Clitocybe nebularis Omphalates illudens	Full recovery
Acromelic acid	Clitocybe acromelalga	Full recovery
Antibodies to Paxillus involutus	Paxillus involutus	Full recovery
Allergic to spores of Lycoperdon species	Lycoperdon species	Full recovery

species are known to be the most fatal. This particular syndrome presents in three distinct clinical phases.

The first phase starts 6 hours after ingestion of the mushroom with cholera -like diarrhoea, vomiting, abdominal pain, and subsequent dehydration.

The second phase begins 24-36 hours where there is laboratory evidence of hepatotoxicity though clinical improvement is observed in patients.

In the third phase, seen after 48 hours is the onset of fulminant hepatitis progressing to hepatic coma, hemorrhage and renal failure, which becomes more evident within 4-7 days, resulting in death.

Seizures, delayed gastroenteritis and liver toxicity: Intake of gyromitra species are known to cause gastroenteritis with severe poisoning causing neurological and hepatic manifestations. The gyromitrin is present in most of the gyromitra mushrooms. The toxicity can be differentiated from that of the amanita species based on seasonal considerations as they grow more in spring and early summer compared to the Amanita species that are seen in the fall of the season. Apart from the seasonal consideration, the 'brain like appearance' of the gyromitra mushroom help in differentiating it from the Amanita species. The clinical manifestations of gyromitrin toxicity includes: delayed gastroenteritis, headache, seizures, hepatitis, hemolysis and methemoglobinemia.

Delayed renal failure: This is seen with the toxins orellanine, cortinarin A, cortinarin B causes interstitial nephritis and tubulointerstitial fibrosis found in mushroom species Cortinarius orellanus, Mycena pura and Omphalatus orarius. Treatment for Cortinarius ingestion requires supportive care for acute kidney injury and hemodialysis should be considered for few individuals.

Delayed rhabdomyolysis is another clinical syndrome seen with Tricholoma equestre species. Onset of symptoms occurs within 24-72 hours after consumption, which results in myalgia, and progressive weakness. On laboratory evaluation there is hyperkalemia with raised creatinine phosphokinase.

Rare manifestations: Other rare manifestations of mushroom poisoning which are less lethal are erythromelalgia, delayed encephalopathy, allergic bronchioalveolitis, and immune mediated hemolytic anemia.

Diagnosis

Any patient presenting to the ED with the delayed onset of vomiting and diarrhoea six hours or more following consumption of foraged mushrooms must be presumed an amatoxin poisoning until proven otherwise. The key element in evaluating a patient with mushroom poisoning includes proper history, identification of the mushroom species, symptoms and signs that leads to a particular syndrome. The commonest wild mushrooms resulting in morbidity and mortality are the amanita species that grows in woodlands, on dead stumps and near pine trees in deciduous forests. Toxicity of most lethal mushrooms occurs 6 hours post ingestion affecting the gastrointestinal tract, liver and the kidneys.

The baseline investigations that can be a guide to the different clinical syndromes includes complete hemogram, renal and liver function tests, PT/INR,

Table 2: Geographic distribution of mushroom poisoning in India

Location	Clinical Syndrome	Possible mushrooms
South India (Eastern Ghats)	Acute gastroenteritis	Omphalotus olivascens, Mycena pura Chlorophyllum molybdites
Karnataka (Mangalore)	Cholinergic excess	Clitocybe species
North India (Himachal Pradesh)	Acute gastroenteritis, liver failure	Amanita species
North east India (Assam, Meghalaya, Mizoram, Manipur)	Acute gastroenteritis, liver failure	Amanita species

*As per case reports and media reports

creatinine kinase, serum lactate at presentation, followed by serial measurement of CMP, lactate, and PT/INR every 6 to 8 hours.

A medical toxicologist and professional mycologist are known to contribute in identification of the toxic mushrooms and their toxins. A rapid and specific diagnostic ELISA test for detection of amatoxin in serum and urine is there but is not available for clinical use.

Management

Supportive care is the mainstay of therapy of most patients with mushroom poisoning. Specific therapy is guided by the clinical presentation (clinical syndrome).

Gastrointestinal decontamination with activated charcoal benefits maximum when patients presents within one hour of the toxin mushroom ingestion. Gastric emptying by gastric lavage or ipecac syrup has shown minimal benefits, with increased risk of aspiration. Elimination enhancement with multiple activated charcoal has been shown to decrease circulation of the amatoxins after ingestion of the toxins. The recommended doses is 50 gm (0.5gm/kg) every four hourly for four days.

Hemodialysis or hemoperfusion do not remove significant amounts of mushroom toxins hence is not recommended for toxin removal unless patients have signs of acute renal failure requiring hemodialysis in the form of hyperkalemia, metabolic acidosis, uremic signs and encephalopathy.

Biliary drainage by interventional radiology (Simple/Serial gallbladder aspiration, percutaneous cholecystostomy), general surgery (open cholecystostomy), or GI (Nasobiliary drainage with suction placed by ERCP) has been demonstrated to be effective in a growing number of case reports. Removing amatoxin laden bile from the gallbladder provides definitive protection to uninvolved hepatocytes by eliminating further enterohepatic exposure to the poison. Simple ultrasound guided gallbladder aspiration appears to be the fastest, safest, easiest, and most efficient means of permanently removing accumulated amatoxin from the biliary tract. It can be accomplished using a transhepatic approach early in the clinical course or via a transperitoneal approach if the INR is above 2. The collected bile sample should be labeled and frozen carefully for subsequent analysis of amatoxin content.

Intravenous Octreotide (200 mcg bolus followed by

50 mcg per hour) helps to keep amatoxin contained in the gallbladder and thus limiting further hepatocyte exposure. Octreotide effectively inhibits bile outflow from the common bile duct and gallbladder by raising pressure at the Sphincter of Oddi and enhances GB filling by reducing GB intraluminal pressure.

SPECIFIC ANTIDOTES IN DIFFERENT TOXINS INDUCED MUSHROOM POISONING

Amanita poisoning

Amatoxin uptake inhibitors like silibinin or intravenous penicillin G have been shown to be associated with higher levels of patients survival. This blockade or inhibition results in the diversion of amatoxin back into the general circulation for renal clearance, therefore maintaining renal function and a brisk urine output is crucial to the success of the drug. The recommended doses for silibinin is 5 mg/kg bolus then followed by 20 mg/kg/day for 6 days or till patient recovers. Intravenous Penicillin G is considered when silibinin is not available given at the dose of 300,000 -1,000,000 units /kg/day as continuous infusion for the same duration. Penicillin G probably acts by competitive inhibition of plasma protein binding of amatoxin and thus causing excess urinary excretion and also as uptake inhibitor. Other amatoxin uptake inhibitors which have been found to be effective include silymarin and ceftazidime. A dose of silymarin is given in high doses 150 -360 mg every 8 hourly upto 2 gm /day for 6 days or till recovers. Injection ceftazidime is also given in high dose of 4 gm every 2 hourly.

Antioxidants are also indicated in amatoxin poisoning as the toxins are known to enhance lipid peroxidation that contributes to membrane instability and cell death. Antioxidant prevents lipid peroxidation. Among the antioxidants injectable N acetylcysteine (NAC) is preferred in the dose 150 mg/kg bolus over 1 hour, followed by 12.5 mg/kg over 4 hours, 6.25 mg /kg over 16 hours.

Gyromitrin toxicity with seizures should receive pyridoxine (70 mg/kg to 5 gm) per day along with anticonvulsant therapy. Pyridoxine acts by reversing pyridoxal 5 phosphate deficiency in the central nervous system mediated by toxic metabolite monomethylhydrazine. Methemoglobinemia also seen in gyromitrin poisoning when detected should receive intravenous methylene blue.

Cholinergic excess from muscarine toxins should receive

atropine or glycopyrrolate. Repeat anticholinergic agent as needed until bronchial secretions have dried.

Supportive care

Vomiting and diarrhoea are caused by most of the toxins containing mushrooms which can be treated with intravenous fluids and antiemetic.

Agitation, delirium and hallucination are treated with benzodiazepines. Seizures caused by mushrooms containing muscimol, ibotenic acid and gyromitrin are treated with short acting benzodiazepines midazolam or lorazepam and if no response phenytoin sodium is considered as per the epilepsy protocol management.

Rhabdomyolysis caused by *tricholoma equestris* species characterized by raised creatinine phosphokinase with urine showing pigmented granular casts, a red or brown color of urine supernatant. The primary treatment is to give aggressive intravenous fluids preferable normal saline 20-40 ml/kg/hour upto 1 litre/hour.

Renal failure when present hemodialysis should be considered in candidates with fluid overload, refractory to diuretics, hyperkalemia, metabolic acidosis and signs of uremia (pericarditis, unexplained decline in mental status).

Fulminant hepatitis when present should prompt the physician for early transfer of patient to a liver transplant center and when patient with hepatotoxicity does not improve even after 4 days of supportive therapy.

CONCLUSION

More studies are required in mushroom poisoning in our country for proper judgment of the types of mushrooms causing morbidity and mortality. Awareness programs in the affected area should be carried out and early supportive therapy should be the goal in affected population.

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