Scientific Foundation SPIROSKI, Skopje, Republic of Macedonia
Open Access Macedonian Journal of Medical Sciences. 2020 Sep 03; 8(E):616-622.
https://doi.org/10.3889/oamjms.2020.4208
eISSN: 1857-9655
Category: *E - Public Health*
Section: *Public Health Disease Control*

A Report on Mushrooms Poisonings in 2018 at the Apulian Regional Poison Center

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Edited by: Sasho Stoleski
Citation: Pennisi L, Lepore A, Gagliano-Candela R, Santacroce L, Charitos IA. A Report on Mushrooms Poisonings in 2018 at the Apulian Regional Poison Center. Open Access Maced J Med Sci. 2020 Sep 03; 8(E):616-622. https://doi.org/10.3889/oamjms.2020.4208
Keywords: Poisoning; Intoxication; Epidemiology; Poison center; Mushroom poisoning
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Received: 17-Dec-2019
Revised: 08-Jan-2020
Accepted: 01-Feb-2020

Funding: This research did not receive any financial support
Competing Interest: The authors have declared that no competing interest exists

Abstract

BACKGROUND: The "Ospedali Riuniti's Poison Center" (Foggia, Italy) provides a 24 h telephone consultation in clinical toxicology to the general public and health-care professionals, including drug information and assessment of the effects of commercial and industrial chemical substances, toxins but also plants and mushrooms. It participates in diagnosis and treatment of the exposure to toxins and toxicants, also throughout its ambulatory activity.

METHODS*:* To report data on the epidemiology of mushroom poisoning in people contacting our Poison Center we made computerized queries and descriptive analyses of the medical records database of the mushroom poisoning in the poison center of Foggia from January 2018 to December 2018.

RESULTS: A total of 69 mushroom poisonings cases were recorded in our poison center the period from January 2018 to December 2018. Our poison center serves all the Italian territory but most of the calls about mushrooms poisonings, in 2018, came from Apulia, Campania, and Basilicata, which are bordering regions of Italy. About 80.2 % of calls were made by the physicians (particularly, 73.9% by emergency room, 18.8% and 4.3% by hospital ward, and 1.4% both by a general practitioner and by the American Sign Language ["ASL"]) and 18.8% by the public. Cooked mushrooms were involved in all the cases (single and multiple species). The most frequent calls were made in the period between September 2018 and December 2018; in the other months, there were only sporadic cases. All were intentional exposures in adults (>18 years).

CONCLUSIONS: Mushroom exposures and poisonings are an important problem in those regions of Italy where many people adventuring in mushroom's research without any license. This fact has contributed substantially to morbidity due to mushroom poisoning. Our database is a valuable national resource for the collection and monitoring of Italian mushroom poisoning cases in 2018 but limited to the people who called our poison center, which is one of the nine poisons centers in Italy. And since in most cases, the mushroom's species remains unknown, it is important to quickly recognize symptoms and most frequent species involved on the Italian territory, in particular in South Italy.

Introduction

Uncontrolled mushrooms are widely available in local markets and street greengrocers; at the same time, many people in Italy are usual to practice the mushrooms research as a recreational activity, without having an official license; an unavoidable effect has been the increase in the number of mushroom poisonings, which is an important cause of access to emergency room. The consequences of mushroom poisoning range from mild, mostly gastrointestinal, disturbances to organ failure, or even death [1], [2], [3]. Differential diagnosis is often a challenge and must consider infective conditions, renal failure, cardiovascular conditions, etc. In addition, in peripheral hospitals, specific laboratory test is not always available, as well as dedicated poison centers. An important objective of a poison center is to provide mushroom poisoning information to health-care professionals, but at the same time, it provides first aid and triage in cases of mushroom poisonings and allows to shorten the time between a suspect ingestion of mushrooms by people who call directly a poison center and the referral of the poisoned patient to the most appropriate health center for the treatment and hospitalization [4]. The clinical staff includes physicians who are board certified in Anesthesia and Intensive Care Medicine and in Clinical Pharmacology and Clinical Toxicology [5]. We use a computerized database which includes toxicological medical records and facilitate quick clinical and epidemiological searches [6], [7].

Patients and Methods

This report analyzes the data of all calls and the clinical toxicological consultations made to the poison center of the "Ospedali Riuniti di Foggia" provided during the year 2018 about mushroom poisonings. Our poison center serves both the general public and health-care

facilities 24 h a day and collects epidemiological data on incidence and trends of poisonings, symptoms, and severity of the intoxications, providing the public people information on how to prevent mushroom poisoning [8].

When the public or health-care professionals call our poison center in Foggia for a medical emergency, the process of consultation starts understanding the patient's condition (conscious, unconscious, gastrointestinal, and/or systemic symptoms), when he ate mushrooms and if he maintains food residues; in this case, we call the mycologist service on call for a specific recognition. If we suspect a serious intoxication, we provide first aid and we referral the patient to the emergency department for evaluation and treatment. The consultation is tailored to the patient's conditions and not to the responsible mushroom because many times the patient does not know the incriminate genus and species and does not maintain food residues, so we cannot identify exactly the cause of poisoning. We record in our database demographic details about patients (caller title, age, and gender of the patient), mushrooms' species involved (if known), circumstances of exposure (at home, at restaurant…), the ingested amount, clinical manifestations, management, evaluation (including laboratory confirmation of exposure such as the urinary "Amanitina test"), and follow-up for moderate to severely poisoned patients [9]. The clinical severity of each case at the time of consultation is graded as minor (local symptoms, self-limited), moderate (with systemic symptoms but not life threatening), major (with life-threatening manifestations), or death [8], [10].

Results

The poison center of Foggia recorded 69 mushroom poisonings cases during 2018.

Figure 1 shows the number of mushroom poisonings cases reported to the poison center from January 2018 to December 2018. This figure clearly shows the peak of mushroom poisonings in the period between September and December, so in autumnal period.

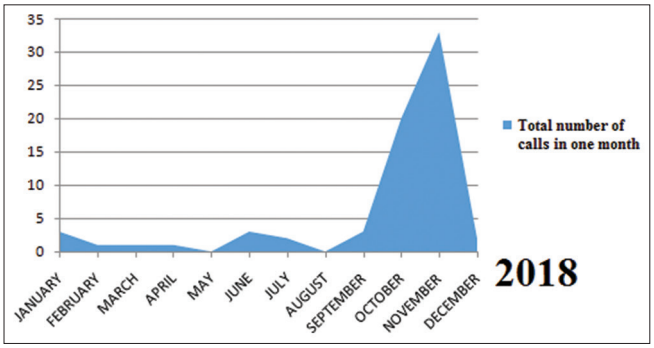

Figure 1: Recorded cases of mushroom poisoning in the period 01 January 2018 - 31 December 2018 at our Poison Center

Figure 2 shows the origin of the calls to the poison center of Foggia regarding mushrooms poisonings in 2018. Most of calls (61) come from Apulia, the region in which our poison center is placed. Five calls come from Campania and other three calls come from Basilicata, which are bordering regions.

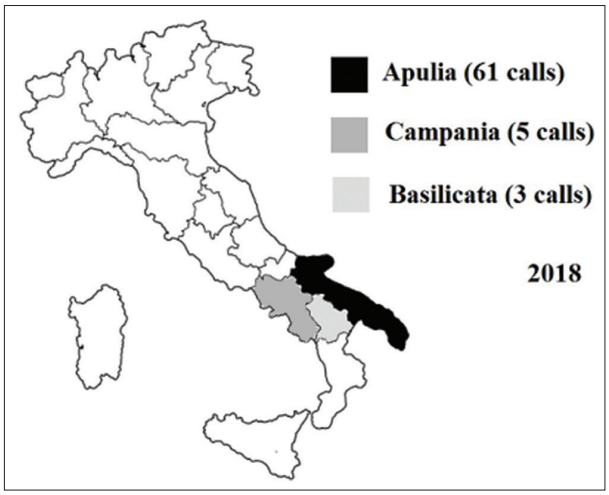

Figure 2: Origin of the calls from different regions of Italy

Figure 3 shows the origin of the calls from different regions of Apulia in 2018. Most of calls come from the cities of Bari (19), Brindisi (14), Foggia (12), and Lecce (11) and their communes. Less calls come from Taranto (4) and Barletta-Andria-Trani provinces (1).

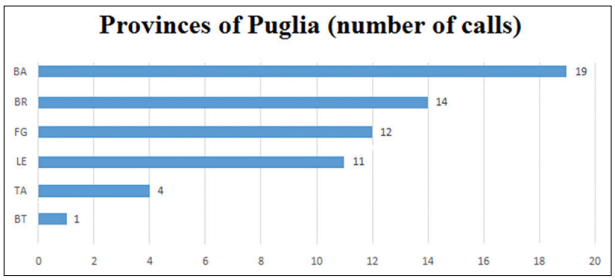

Figure 3: Origin of the calls from different Apulian provinces

Figure 4 shows the origin of the calls from different regions of Basilicata in 2018. We received three calls from the city of Matera and its communes. Instead, Figure 5 shows the origin of the calls from different regions of Campania: We received three calls from the city of Benevento and other two calls from the city of Avellino and their communes.

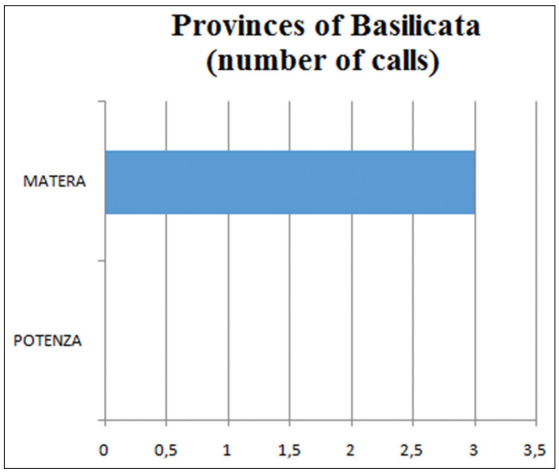

Figure 4: The origin of the calls from different regions: Basilicata

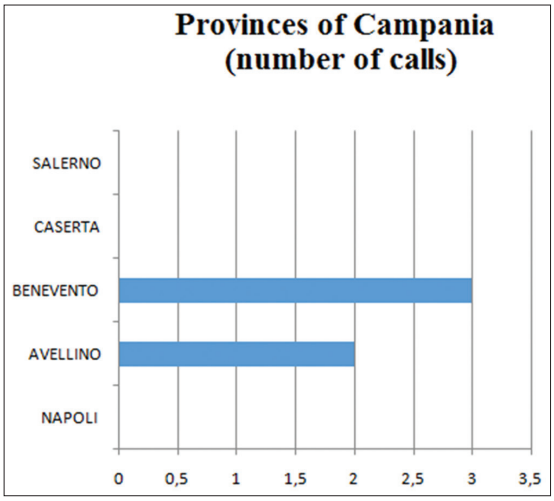

Figure 5: Calls from different provinces of Basilicata

Table 1 illustrates the various callers and sites of exposure. The majority of calls (73.9%) came from the emergency room, but also by the hospital physicians (4.3%), general practitioners (1.4%), and ASL (1.4%). The percentage of calls from public is only the 18.8%. The most common site of exposure is the home (92.7%) followed by restaurants (4.3%) or outdoor picnics. The higher percentage of cases at home let we think that mushroom intoxications occurs frequently with uncontrolled mushrooms which are picked from the woods. Hence, we insist that only controlled mushrooms must be eaten by non-expert people [1].

Table 1: Site of caller and site of mushroom exposures

Caller %		Site of exposure (%)	
Emergency room	51 (73.9)	Home	64 (92.7)
Public	13 (18.8)	Restaurants	3 (4.3)
Hospital ward	3 (4.3)	Outdoor	2 (2.8)
General practitioner	1 (1.4)		
American Sign Language	1 (1.4)		

Table 2 shows the referred symptoms at the moment of the call at the poison center in 2018 after a menu based on mushrooms. Eleven people were asymptomatic during the call, but there was a strong suspect of food intoxication because they have symptoms previously. Fifty-eight patients were symptomatic: All of them reported gastrointestinal symptoms (100%) such as vomit and diarrhea, 13.7% developed a skin rash, and 12.06% showed central nervous system symptoms; less percentage of patients had neuromuscular (8.6%), metabolic (3.4%), ocular (3.4%), and cardiovascular (1.7%) symptoms or signs.

Table 2: Symptoms reported at the time of the call

Asymptomatic (%)		Symptomatic (%)	
Total	11	Total	58
		Gastrointestinal	58
		Skin	8 (13.7)
		C.N.S.	7 (12.06)
		Neuromuscular	5 (8.6)
		Metabolic	2 (3.4)
		Ocular	2 (3.4)
		Cardiovascular	1 (1.7)

Table 3 shows a summary of the total number of unidentified or identify genus and species of mushrooms regarding each single call with mushrooms ingestion in the anamnesis. Most times, how we can note in the first row of Table 3, people say that they have just eaten "mushrooms," but they cannot specify what kind of genus or species. In the others rows of the table, an indicative list of edible or toxic mushrooms is provided: In some cases, the real cause of the mushroom poisoning has been identified by the mycologist service thanks to the food residues provided by the person calling or an accurate description of the mushroom's characteristics, in other case, we are not able to identify the real poisonous mushroom, but we can just report the genus and species that the poisoned patients thought that they had found in the woods but they do not recognize as a toxic one. In 21 cases, we suggested to research the *amanitin* in urine using a specific urinary diagnostic test: Eleven patients resulted positive to the test [11], [12]. In all cases with a positive result of this test or with evident symptoms of intoxication, we quickly started treating patients with L-acetylcysteine, repeated hematochemical tests and with liver ultrasound tests. All patients were observed through various follow-ups overtime both at home and in hospital for the hospitalized patients.

Table 3: Total number of unidentified or identify cases of mushroom poisoning

Mushrooms (without specifying)	30
Boletus edulis	11
Cantharellus cibarius	5
Lepiota helveola	5
Lactarius zonarius	4
Agaricus campestris	3
Russula torulosa	3
Clitocybe nebularis	3
Omphalotus olearius	2
Lactarius sanguifluus	2
Calocybe gambosa	2
Rubroboletus pulchrotinctus	2
Amanita pantherina	2
Amanita citrina	2
Russula virescens	1
Clitocybe gibba	1
Armillaria mellea	1

Discussion

Our casuistry reports the total number of calls received by our poison center of the "*Ospedali Riuniti*" in Foggia about mushroom intoxications in 2018. Our database is a valuable national resource for the collection and monitoring of Italian mushroom poisoning cases in 2018 but limited to the people who called our poison center. However, compared to the previous years, there has been a rise in cases compared to 2017 (Figure 6). During the year 2018, we received 69 calls by people who had gastrointestinal and systemic symptoms after they ate a menu based on mushrooms or by asymptomatic people at the moment they call but with symptoms in the previous hours or day, scared about their possible intoxication; in other cases, the calls directly came from physicians who called us asking information about how to treat poisoned patients in the emergency room or in the hospital ward. As we already said, there are nine poison centers extensively covering the whole of Italy, so we

received calls from three regions: Mainly from Apulia, but also from Basilicata and from Campania.

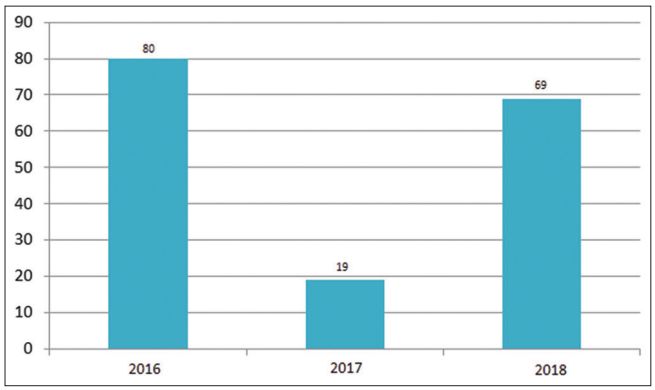

Figure 6: Number of mushroom poisonings cases from 2016 to 2018

Symptoms of mushroom poisoning may vary from gastrointestinal disorders upset to organ failure resulting in death. Serious symptoms can occur immediately after eating, but sometimes the toxin attacks the liver or kidney days or weeks later. Most toxic mushrooms contain gastrointestinal irritants that cause nausea, vomiting, and diarrhea. However, there are a number of recognized mushroom toxins with specific, and sometimes deadly, effects: Extreme gastrointestinal upset, brain damage, seizures, hemolysis, metabolic failure, CNS depression, and hallucinations [13], [14], [15], [16], [17], [18]; the most common species in our territory are *Amanita phalloides*, *Amanita muscaria*, and *Amanita pantherina* [19]. It is very important, when somebody call us asking help about their symptoms or just for information, to establish what the situation is and its potential evolution in few hours, referring our patients to the hospital, if it is necessary. However, the risk of intoxication and poisoning due to mushrooms consumption is common worldwide [8], [20], [21], [22], [23].

The dangerous mushrooms can give two main clinical syndromes, depending on the time of ingestion: Long latency, more severe, from 4 (6) to 24 h and more (more days, 1–3 weeks) and short latency from a few minutes to a 4–6 h. The symptoms are various and related to the fungal species involved; in some serious cases, they can lead to an organ damage as the liver or kidney. As we mentioned, there are a variety of poisonous mushrooms as the Amanita genera, in particular, *A. phalloides* present in our territory, which causes precisely the long latency syndromes, the phalloidin syndrome which is may be fatal in 10–40% of intoxication cases. However, this syndrome is determined by the ingestion of various genus of mushrooms such as the genus Amanita (*A. phalloides, Amanita verna,* and *Amanita virosa*), the genus Lepiota (*Lepiota helveola, Lepiota pseudohelveola, Lepiota brunneoincarnata, Lepiota josserandii,* and probably others), and the genus Galerina (*Galerina marginata* and *Galerina autumnalis*). The main biotoxins are two phallotoxins: Virotoxins and amatoxins [14], [24], [25].

The phallotoxins are seven different bicyclic heptapeptide compounds (phalloidin, phalloin, prophallin, phallisin, phallacin, phallacidin, and phallisacin); the virotoxins are monocyclic peptides formed by five compounds: Alaviroidin, viroisin, deoxoviroisin, viroidin, and deoxoviroidin, and the amatoxins, responsible for the syndrome, are nine bicyclic octapeptides (α-amanitin, β-amanitin, γ-amanitin, ε-amanitin, amanin, amaninamide, amanullin, amanullinic acid, and proamanullin) and the lethal dose of amatoxins in humans has been quantified at 0.1 mg/kg of weight body [24], [25], [26]. They are resistant to boiling, drying, and gastric juices and are rapidly absorbed from the gastrointestinal tract, do not undergo metabolic alterations in the human body, persist in the circulation for about 36 h from ingestion, and are eliminated intact with urine and feces. The target organ is the liver where they reach the liver cell with a mechanism similar to the transport of bile salts but in part, they are then reabsorbed by the intestine thus returning to the circulation, creating the so-called enterohepatic recirculation. In the liver, they cause blocking of protein synthesis because the inhibition of the RNA-polymerase II enzyme inside the cell nucleus, interfering in the transcription of messenger RNA from DNA with consequent cell death. Other mechanisms have been proposed that cause cellular apoptosis such as the oxidative stress damage that the amatoxin reacts together with tumor necrosis factor, and the translocation of the human p53 cellular tumor antigen to the mitochondria which changes the functionality of the mitochondrial membrane. Histologically, the damage occurs with vacuolar degeneration of hepatocytes and diffuses centrilobular necrosis while in the kidneys, we have tubular necrosis. The amatoxins are then excreted in the urine up to 48 h after ingestion and in traces within 73 h; in biliary secretions and in the intestinal tract, they can also be present after 4–5 days [11], [14], [24], [25]. The course of the disease is generally characterized after 6–24 h by three phases: (a) Gastrointestinal: Characterized by abdominal pain, vomiting, and profuse diarrhea, which quickly lead to severe dehydration with alteration of the electrolytes (potassium, sodium, and chlorine) and the loss of bicarbonates which leads to metabolic acidosis. If the fluids are not replenished quickly, a renal failure can result in shock with the risk of death; (b) the remission phase occurs in the 2nd and 3rd days, there is an improvement in the gastrointestinal picture, but the damage to the liver begins to show up; (c) hepatorenal phase with damage to these organs. Liver damage can evolve rapidly into acute liver failure with increased bilirubin, increases liver enzymes, impaired coagulation, accompanied by kidney failure, and shock. In less severe intoxications, after 5–6 days from ingestion, there is a progressive healing and liver function returns to normal within about 30 days. In severe intoxications, within 4–5 days from intoxication (if there are no initial signs of recovery such as coagulation stability), an unfavorable evolution can occur with progressive worsening of the clinical picture that can lead the patient to liver transplant or to death [19], [25]. Several antidotes are used to counteract toxicity, such

as N-acetylcysteine and silybin, benzylpenicillin, and ceftazidime, but their use is still controversial because for none of these it has been clearly demonstrated or approved that it has great clinical efficacy and also because there is still a high mortality rate in this mushroom poisoning. Other treatments would be for the prevention of amatoxins absorption, gastric lavage and activated charcoal, and forced diuresis. They were also used for the elimination of absorbed amatoxins hemodialysis, hemofiltration, hemoperfusion, and plasmapheresis. If necessary, the treatment may also include fresh frozen plasma and intravenous Vitamin K. Instead, the liver transplant occurs during acute liver failure [25], [27], [28], [29]. In addition to the reintegration of liquids and electrolytes in the first phase of intoxication, the usefulness of probiotics has proved in states of oxidative stress, profuse diarrhea, inflammatory states, infections, etc. [30], [31], [32], [33]. From a laboratory point of view, blood count, liver and kidney function, ammonia, electrolytes, amylase, lipase, and coagulation test panels are mainly performed. The prognosis is primarily related to the timeliness of the therapy and the health conditions and age of the patient. Survival then depends not only on liver damage and cell regeneration capacity but also on the therapeutic conduct of complications that may develop [25], [26].

Due to the difficult in differential diagnosis, i.e., food intoxications or pre-septic conditions, a large number of laboratory tests have been proposed to test the patients with suspect symptoms, and the pathophysiologic and prognostic value of some nutrients and serum molecules have been tested [11], [12], [24], [34], [35], [36], [37], [38], [39], [40], [41].

It is important to underline the guidelines to avoid poisoning due to consumption of the wrong type of mushrooms to all interested people and to health professionals so that they know how to act when poisoning occurs, thus helping to prevent and reduce the number of deaths, the secondary effects, and the complications caused by different poisons and their accompanying syndromes. In general, it is advisable to eat mushrooms only if those who reap them are a local mushroom expert with an official license (after attending an official course about mushrooms' classifications, characteristics, and security for human consumption). In these courses, to prevent mushroom poisoning, mushroom gatherers familiarize themselves with the mushrooms they intend to collect, as well as with any similar-looking toxic species. If it is impossible to verify every identifying characteristic, it is important to throw it out. Moreover, mushroom intoxications can occur not only for poisonings species but also with mushrooms not well cooked (because heat labile toxins are eliminated by cooking), not toxic but eaten in large quantity (because indigestible) or for food allergies [24], [34].

Conclusions

Mushroom poisoning currently remains a harmful and life threatening condition. Most cases occur in autumn and early winter, when mushrooms are abundant and many people research and collect them, often lacking in distinguishing edible and poisonous mushrooms, or without requiring a subsequent mycological examination. Any mushroom poisoning is characterized by a variable and sometimes rapidly evolving clinical picture, and always requires a timely clinical evaluation to use specific diagnostic and therapeutic protocols that can save the patients. The experience of our Poison Center demonstrates how the correct and rapid recognition of possible mushroom poisoning can improve the prognosis of patients.

Acknowledgment

The authors strongly acknowledge Dr. Luigi Galati, MD, for his effective participation in data collection at the Emergency Service – Poisoning Center at Ospedali Riuniti of Foggia, Italy.

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