Factors Affecting Mortality and Complications in Mushroom Poisonings Over a 20 Year Period: A Report from Central Anatolia

Yirmi Yılda Mantar Zehirlenmelerinde Mortalite ve Komplikasyonu Etkileyen Faktörler: Anadolu’dan Bir Rapor

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SUMMARY

Objectives
Mushroom poisoning (MP) is one of the world’s leading seasonal and regional health problems. The aim of this study was to analyze the relationship between clinical factors and outcomes of mushroom poisoning.

Methods
The study was conducted in the emergency department. The patients who presented between January 1st, 1991 and December 31, 2010 were retrospectively reviewed.

Results
599 MP cases were enrolled into the statistical analysis. The elderly group had a higher rate of mortality (8.8%) and complications (12.3%) (p=0.005) (OR 3.98, 95% CI: 1.9291 to 8.2290; p=0.0002). The patients who presented in summer had a higher rate of mortality (9.5%) and complications (11.9%) (p<0.001). (OR: 3.83, 95% CI 1.7068 to 8.6074, p=0.0011). The rate of mortality and complications in patients who had eaten self-harvested wild mushrooms (WM) was 6.8%, while those who purchased WM had a mortality and complication rate of 15.2% (p=0.016). (Purchased WM OR 2.46, 95% CI 1.1609 to 5.2353, p=0.0189). The rate of mortality and complications in the patients who presented with gastrointestinal symptoms was 9.9% (OR: 3.98, 95% CI 1.5503 to 10.2679; p=0.0041).

Conclusions
Factors such as being elderly, summer season, purchased WM, and gastrointestinal symptoms were significantly associated with mortality and complications in our study.

Key words: Elderly; emergency department; mushroom; poisoning; summer season.

ÖZET

Amaç
Mantar zehirlenmeleri (MZ) dünyanın önde gelen mevsimsel ve bölgesel sağlık problemidir. Bu araştırmanın amacı MZ’de klinik faktörlerle sonuçlar arasındaki ilişkiyi incelmektir.

Gereç ve Yöntem

Bulgular
599 MZ olgusu araştırımaya dahil edildi. Yaşlı hastalar daha yüksek mortalite (%8.8) ve komplikasyon (%12.3) oranına sahiptiler (p=0.005). (Odd oranı [OO]: 3.98, %95 [Güven Aralığı] GA 1.9291 – 8.2290, p=0.0002). Yaz aylarında başvuran hastalar daha yüksek mortalite (%9.5) ve komplikasyon (%11.9) sahiptiler (OO: 3.83, %95 GA 1.7068 to 8.6074, p=0.0011). Mantarları kendi toplayıp yemiş olan hastalarda mortalite ve komplikasyon oranı %6.8 iken bu oran satın alınmış vahşi mantarlarda %15.2 idi (p=0.016), (satın alınan mantarlar için OO: 2.46, %95 GA 1.1609 – 5.2353, p=0.0189). Gastrointestinal semptomları olan hastaların mortalite ve komplikasyon oranı %9.9 olarak saptandi (OO: 3.98, %95 GA 1.5503 – 10.2679, p=0.0041).

Sonuç
Yaşlılık, yaz mevsimi, satın alınmış vahşi mantarlar ve gastrointestinal semptomlar mortalite ve komplikasyonlar ile anlamlı ilişki göstermiştir.

Anahtar sözcükler: Yaşlılık; acil servis; mantar; zehirlenme; yaz mevsimi.
Introduction
Mushroom poisoning (MP) is one of the world’s leading seasonal and regional health problems. Eating poisonous wild mushrooms (WM) can lead to unwanted reactions such as gastroenteritis or more severe pathologies including fatal liver failure. Fatal MP is very well described in the literature. Fortunately, though, the majority of MP cases have a good prognosis.

The Central Anatolian region of Turkey has considerable reputation in terms of MP. MP can be commonly observed in Europe, Anatolia and the Middle East, and the reports from these regions, including incidence and prognosis, have significant differences.

In our previous studies, we tried to call attention to different aspects of MP. These studies consisted of short-term data and had no detailed evaluation of the relationship between clinical data and outcome measures (mortality and/or complications). As far as we are aware, in the English literature, the number of studies evaluating this relationship and prognostic criteria is limited. Additionally, other studies have concentrated on different variables.

The aim of our study was to analyze the relationship between clinical factors and outcomes of MP. In this study, we report MP cases admitted to our hospital serving four Anatolian cities with a total population of approximately two and a half million people over the last 20 years.

Materials and Methods
Hospital
The study was conducted in the emergency department of the university hospital, which is a tertiary care center for all medical and trauma patients, as well as for toxicology and environmental cases.

Patients
The patients who presented or transferred to the emergency department and were diagnosed as MP between January 1st, 1991 and December 31, 2010 were included in the study group. The patients included into the study group were selected according to the inclusion criteria.

Data acquisition
ICD-10 and 9 codes of MP were entered into the hospital information system. The list of cases was obtained by use of these codes. The detailed information of cases was found retrospectively in electronic health records as well as in archived patient files for cases admitted before 2007.

Basic descriptive data of cases including age (age groups 0-17: child and adolescent, 18-39: young adults, 40-64: middle age, 65 and older: elderly), gender, presenting months and seasons, presenting symptoms (neurological, gastro-intestinal, and other), how WM were obtained (self harvest from nature, purchased from public market), the means of admission (direct presentation or transferred), laboratory results (Blood Urea Nitrogen (BUN, mg/dL), Creatinine (Cr, mg/dL), alanine aminotransferase (ALT, U/L), aspartate aminotransferase (AST, U/L), clinical care area (emergency department, ward, or intensive care unit [ICU]), length of stay in the hospital, and outcome (mortality, complication (end stage renal failure, seizure disorder, etc.), full recovery) were collected.

Inclusion and Exclusion Criteria
The patients who had the above clinical/laboratory details in their files were included into the study. The patients who had co-ingestion of drugs in overdose, drugs of abuse, missing clinical follow-up or did not have the above clinical/laboratory details in their files were excluded from the study.

Outcome Measures
Patient data were evaluated for their relationships with mortality, complications (end stage renal failure, seizure disorder, etc.), and full recovery.

Data Analysis
Statistical Package for the Social Sciences (SPSS, version 18) and Statistical Analysis and Graphics Software (NCSS 2007) were used for statistical analyses. Chi-Square and the Fisher Exact test were used for descriptive analyses. Kolmogorov-Smirnov test was used to show the distribution of the data. Mann-Whitney U-test in binary groups and Kruskal-Wallis One Way Analyses of Variance test for three or more groups of data were used, as the data did not show a normal distribution. Odds ratio (OR) was calculated for variables that may affect the outcome, such as age, presenting symptoms, the way of obtaining WM, and admission. A p-value less than 0.05 was accepted as significant. SD: standard deviation, SE: standard error.

Results
721 MP cases were admitted to the hospital within a period of 20 years. 117 cases who did not have clinical/laboratory information in their files and five patients who had been transferred to different cities were removed from the study. 599 cases were enrolled into the statistical analyses.
Gender and Age Groups

There were 319 females (53.3%) and 280 males in the study. The mean age of males and females were similar. According to age groups, there were 162 (27.0%) cases in children and adolescents, 187 (31.2%) cases in young adults, 193 (32.2%) cases were in middle-aged adults, and 57 (9.5%) in the elderly. Comparison data on gender and age groups are presented in Table 1. Although distributions of genders were similar in three age groups, the number of female patients in the young adult group was significantly higher (120, 64.2%) ($\chi^2=13.56, p=0.004$).

There were no significant differences between genders and among the age groups for patients’ presenting season, the means of obtaining WM, and symptoms. There were no differences between genders for distribution of clinical care area and outcome. However, there was a significant difference among the age groups for distribution in the clinical care area. The child and adolescent group was mainly treated in the ward area (128 cases, 79.0%) while 43 cases (75.4%) from the elderly group received medical care in the ICU ($\chi^2=325.932, p<0.001$). The elderly group had a higher rate of mortality (8.8%) and complications (12.3%) than the other age groups ($\chi^2=18.664, p=0.005$). The odds ratio (OR) was 3.98 (95% CI: 1.9291 to 8.2290, Z = 3.736, p=0.0002).

The mean ages of the patients in mortality, complication and full recovery groups were significantly different (41.50 [SE: 4.45], 44.91 [SE: 4.26], 33.98 [SE: 0.88] respectively, $\chi^2=6.429904, p=0.0401$).

Presenting Season

The seasonal distribution of MP showed a binary peak. Spring (April, May, June) had the highest number of patients (367 cases, 61.3%). Autumn (October, November, December) was the second highest season with 166 cases (27.7%). The highest number of patients was seen in June (237, 39.5%).

### Table 1. Comparison data on gender and age groups

<table>
<thead>
<tr>
<th>Gender</th>
<th>Age Group (years)</th>
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<tbody>
<tr>
<td></td>
<td>0-17</td>
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<tr>
<td><strong>Female</strong></td>
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</tr>
<tr>
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<td>319</td>
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<tr>
<td>Mean age (SD)</td>
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<tr>
<td><strong>Male</strong></td>
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<tr>
<td>Winter</td>
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<tr>
<td>Spring</td>
<td>198</td>
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<tr>
<td>Summer</td>
<td>20</td>
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<tr>
<td>Autumn</td>
<td>89</td>
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<tr>
<td>Obtaining WM</td>
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<td>Purchased from public market</td>
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<td>Presenting symptoms</td>
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<td>Neurologic</td>
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<td>Gastrointestinal</td>
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<td>Other</td>
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<td>Ward</td>
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<tr>
<td>ICU</td>
<td>176</td>
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<tr>
<td>Outcome</td>
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<tr>
<td>Full recovery</td>
<td>295</td>
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<tr>
<td>Mortality</td>
<td>11</td>
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<tr>
<td>Complications*</td>
<td>13</td>
</tr>
</tbody>
</table>

*End stage renal failure in 23 patients and permanent seizure in one patient were complications in our study.
Neurologic symptoms were higher in autumn (109 of 133 cases, 82.0%). Gastrointestinal symptoms were common in spring (218 of 413 cases, 52.8%) and autumn (143 of 413 cases, 34.6%). Presenting symptoms differed significantly among seasons ($\chi^2=43.578$, $p<0.001$).

In winter, complications were seen in only two cases, while there were no fatal cases. The patients who presented in summer had a higher rate of mortality (9.5%) and complications (11.9%) than other seasons ($\chi^2=28.108$, $p<0.001$). The OR was found to be 3.83 (95% CI: 1.7068 to 8.6074, Z=3.255, $p=0.0041$). The rate of mortality and complications in the patients who had eaten self-harvested WM was 6.8% (36 of 533 cases, 19 mortality, 17 complications), while the group that purchased WM had a 15.2% rate of mortality and complications (10 of 66 cases, 3 mortality, 7 complications ($\chi^2=5.841$, $p=0.016$). The OR of purchased WM was found to be 2.46 (95% CI: 1.1609 to 5.2353, Z=3.255, $p=0.0189$).

The means of obtaining mushrooms

The majority of cases (foragers) had obtained and eaten self-harvested WM (533 cases, 89.0%), while 66 patients (11.0%) had eaten WM purchased from a public market.

282 patients who had eaten self-harvested WM were treated in the ICU (52.9%). The ICU admission rate was higher in patients (38 cases, 57.6%) who had eaten purchased WM ($\chi^2=7.084$, $p=0.029$).

The outcome was also significantly different between these two groups. The rate of mortality and complications in the patients who had eaten self-harvested WM was 6.8% (36 of 533 cases, 19 mortality, 17 complications), while the group that purchased WM had a 15.2% rate of mortality and complications (10 of 66 cases, 3 mortality, 7 complications ($\chi^2=5.841$, $p=0.016$). The OR of purchased WM was found to be 2.46 (95% CI: 1.1609 to 5.2353, Z=3.255, $p=0.0189$).

Presenting symptoms

Patients described gastrointestinal (413 cases, 68.9%), neurologic (133 cases, 22.2%) or other symptoms (53 cases, 8.8%) as their first presenting symptom. Among all symptoms, nausea was the most common (322 cases, 53.8%), followed by light-headedness and vomiting (13.4% and 8.3%, respectively).

The rate of mortality and complications in the patients who presented with gastrointestinal symptoms was 9.9% (41 of 413 cases, 20 mortality, 21 complications). The OR of gastrointestinal symptoms for mortality and complications was 3.98 (95% CI: 1.5503 to 10.2679, Z=2.869, $p=0.0041$). The rate of mortality and complications was lower in patients with neurological symptoms (3.0%) and the other symptoms (1.9%). There was a significant difference for mortality and complications among the groups ($\chi^2=9.547$, $p=0.008$).

Admission to the hospital and length of stay

121 (20.2%) patients directly presented to our emergency department. The majority of cases had first been admitted to primary or secondary health care centers (478 cases, 79.8%), and then were transferred to our emergency department. Forty-seven of the 121 (38.8%) directly presented cases were admitted to the ICU, while the ICU admission rate was 57.1% in transferred cases ($\chi^2=16.620$, $p<0.001$).

The patients who were admitted had clinical care in three different locations: 320 cases (53.4%) in the ICU, 156 cases (26.0%) in the ward, and 123 cases (20.5%) in the emergency department.

The hospital length of stay of transferred cases (mean: 3.24 (CI: 2.86-3.61); median: 2) was significantly higher than in the directly presented group (mean: 2.42 (CI: 2.02-2.83); median: 2) ($p<0.001$).

The elderly group had 5.80 (SE: 0.50) days of hospital stay. Child and adolescent, young adult, and middle age groups had 2.90 (SE: 0.29), 2.51 (SE: 0.27), and 2.95 (SE: 0.27) days, respectively. There was a significant difference among the age groups for length of hospital stay ($\chi^2=18.36774$, $p<0.001$).

The mean length of stay of fully recovered patients was 2.76 (SE: 0.15) days, while the mean lengths of stay were 7.31 (SE: 0.79) days in fatal cases and 6.37 (SE: 0.76) days in complicated cases ($\chi^2=5.908688$, $p=0.043$).

Mortality and complications in directly presented cases were 0.8% (one case) and 3.3% (four cases) respectively. Transferred cases had higher rates of mortality (21 cases, 4.4%) and complications (20 cases, 4.2%). Although there was a difference between the two groups, it was not significant. The OR for transferred cases was found to be 2.17, but it was also not significant (95% CI: 0.8412 to 5.6324, Z=1.603, $p=0.1088$).

Laboratory Results

BUN, Cr, AST and ALT levels of all cases were evaluated. All laboratory levels showed differences between outcome groups. The levels evaluated were the first laboratory levels obtained in the emergency department.

Mean BUN levels by outcome were found as follows: 16.14 (SE: 0.58) in the full-recovery group, 35.09 (SE: 2.93) in the mortality group, and 61.54 (SE: 2.80) in the complication group ($\chi^2=59.43019$, $p<0.001$). Creatinine levels were 1.10 (SE: 0.29) in the full-recovery group, 2.19 (SE: 0.41) in the mortality group, and 4.27 (SE: 0.39) in the complication group ($\chi^2=58.21726$, $p<0.001$). AST levels were 63.79 (SE: 28.66) in the full-recovery group, 2983.09 (SE: 143.73) in the mortality group, and 313.58 (SE: 137.61) in the complication group ($\chi^2=83.94112$, $p<0.001$). ALT levels were 62.83 (SE: 31.01) in the full-recovery group, 3056.95 (SE: 155.48) in the mortality group, and 480.20 (SE: 148.86) in the complication group ($\chi^2=74.45051$, $p<0.001$).
Discussion

Most articles on MP are case reports or series. The effects of demographic data and other key information on outcomes are not well studied or published in the literature. There are many factors that affect the outcome of MP, including type of ingested mushroom, location, the amount of toxin delivered, laboratory results, clinical findings, medical treatment given, hemodialysis, or liver transplantation. In addition to many known details of this toxicity, MP still has some diagnostic and treatment dilemmas for medical professionals.

Although MP has a complex and challenging clinical progress, mortality is seen very rarely. In 2010, 6,275 MP cases were reported to the American Association of Poison Control Centers (AAPCC). Only one death was reported.

Unfortunately, there is no center collecting poisoning reports in Europe and in the Middle East. There are also no annually published poisoning reports in these regions. Therefore, it is difficult to estimate the true incidence of MP in this part of the world. According to the report of one of the regional poison information centers in our country, MP accounted for 1.2% (799 cases) of the 65,176 poisoning cases in the last 14 years. Only one death was reported in this report, and the source was an unknown type of WM. Although public awareness about WM and a more skeptical approach by physicians to MP has decreased mortality, some unpublished reports of deaths have been declared to be fatal MP cases in the Assam area of India in 2008.

There are different reasons for exposure to WM in different age groups. Children may be unintentionally poisoned by eating WM found in outdoor areas. However, adults are more prone to collect and eat WM intentionally. Schenk-Jaeger et al. reported that 86.4% of their cases were accidental exposure to mushrooms. They also report abuse and suicide cases (12.8% and 6.3%, respectively). We did not determine abuse or suicidal ingestion in our cases. Hocaoglu's study also had the same finding.

The number of female patients was found to be higher in our study as in some other reported studies. Hocaoglu reported a female/male ratio of 1.24. Another report from northeast part of Turkey found 67.5% female patients. In the present study, we have no strong data showing a relationship between gender and outcome.

We can estimate risk groups for poisoning because of their physiologic and metabolic factors or comorbidities. Children and elderly are at the greatest risk for toxicity and the worst outcomes for all types of poisoning. Therefore, evaluation of the outcome among the age groups was one of the main focuses of our study. In 2010, AAPCC reported that 70.1% of all MP cases were in patients with an age of 19 years or less. Although our study did not use the same age ranges as the AAPCC report, we found 27.0% of cases in those patients less than 18 years old. This demonstrated a difference in the age distribution of MP cases between countries. Mortality and complication rate (21.3%) in the elderly group (65 and older) in our study was higher than the other age groups, with an OR of 3.98. In patients under 19 years old, we found a 9.4% rate of mortality and complications. The mean age of full-recovery cases was also significantly lower than the mortality and complication groups. According to this finding, we may suggest that MP does not have the worst outcomes in children and adolescents. However, mortality and complication rates rise with increasing age according to our results and our previous report. Because our study showed that elderly patients have the worst outcomes, emergency physicians and ICU physicians should pay special attention in taking care of this age group.

MP has some seasonal variations in literature. Schenk-Jaeger et al. reported that there is one peak in their study, occurring in late summer. In Ishihara's report, summer and early autumn were the most common seasons for MP. MP in our region has a binary peak, in spring and autumn. However, mortality and complication rates were highest in summer (total 21.4%). Most WM poisoning affects the gastrointestinal system, and patients present with nausea, vomiting or diarrhea. The most serious effect of MP is on the kidneys and liver. Deterioration of these two important organ functions and failure to recover lead to mortality or irreversible complications such as permanent renal failure. Dehydration is one of the main problems, and it worsens renal function. Inadequate supportive treatment may lead to renal failure. This may affect the outcome, especially in elderly patients. Cases of acute prerenal failure following dehydration are observed not only in elderly patients, but also in young and previously healthy patients.

Eating WM in our country is still a quite common habit. WMs are also commonly sold in public markets, and there are no regional or national regulations to control it. Yardan et al. showed that 87.7% of patients had collected and ate WM, while only 12.3% had purchased WM from a local bazaar. These findings are quite similar to our results. Foragers usually pick WM from open rural fields, woodlands, gardens, or roadsides, then cook and eat. This habit is also widespread in European and Middle Eastern countries. Unfortunately, we found higher mortality and complications in patients who purchased WM from public markets. This is one of the main issues of public health in many countries. Emergency physicians may play a more active role in educating the public on MP.

MP may present varying grades of gastrointestinal and
neurologic symptoms and hepatic/renal involvement depending on the type and amount of mushroom consumed. Gastrointestinal symptoms were the most prominent complaints in our patients. We found that gastrointestinal symptoms have higher mortality and complication rates. Most reports indicate that gastrointestinal symptoms, especially nausea, vomiting and diarrhea, are prominent symptoms. Nausea and vomiting were found in 86.8% and 79.8% of cases in the middle Black Sea region of Turkey. Nausea and vomiting were determined in 93.8% of cases in another report. A. phalloides is one of the well-known toxic mushrooms which cause these symptoms. It is also considered the sole cause of liver damage. Differentiating benign gastroenteritis from potentially life-threatening A. phalloides (amanitin) poisoning is critical for health care professionals. A. phalloides causes these symptoms, as do other types of mushrooms, and inadequate treatment or delayed diagnosis can increase the chance of mortality and complications. In the literature, A. phalloides toxicity is responsible for 90% of fatal MP. Liver failure because of toxic mushrooms may be fatal if the organ transplantation cannot be arranged. We have Amanita, Gyromitra, Inocybe and Omphalatus species in our region. The majority of deaths are thought to be due to Amanita. However, diagnostic typing of consumed mushrooms was unavailable in our cases, and this is a well-known problem in MP in all countries. The AAPCC reported an unknown mushroom type in 79.3% of cases in 2010.

Patients who were transferred from other health care centers were a significant majority of our cases (79.8%). In our previous studies, we have found and published higher mortality and complication rates in patients admitted to and cared for in another hospital for couple days before being transferred to our emergency department. Unfortunately, we have no data on the previous treatments used in such cases, and we cannot perform a detailed discussion on the treatments of transferred patients that may affect outcome. However, transferred patients had higher ICU admissions, longer lengths of stay, and higher mortality and complication rates in our study, and these results suggest that they may not receive enough supportive treatment in previous facilities and/or delayed transfer. Our mortality (3.7%) and complication (4.0%) rate is higher than some other reports. This might be due to medical treatment initiated relatively late in previous health care centers. Yardan et al. reported three deaths in their hospital (0.9%) in six years.

In a regional poison center report, 91.2% of cases were observed and had medical care in emergency departments. In our study, this percentage was 20.5%. They also reported that 3.3% of cases had ward and ICU admission, but this rate was 79.4% in our study. We transferred five cases (0.8%) to different hospitals that had facilities for liver transplantation. The transfer rate was reported as 5.4% in Hocaoglu’s report. We believe that this report reflects the regional fact more rationally. Regional and institutional differences for health care facilities affect patient care and outcomes in MP. Unfortunately, there is no current MP guideline in the English literature, so each institution and region must create its own specific approach to these cases.

Laboratory results (BUN, Cr, ALT, AST) were higher in fatal and complicated cases in our study. Trabulus et al. described the factors associated with greater likelihood of death such as low sodium values and high urea, AST, ALT, total bilirubin, lactate dehydrogenase, prothrombin time, international normalized ratio (INR), and activated partial thromboplastin time values. Some laboratory (INR, etc.) and clinical (encephalopathy, etc.) parameters have also been reported as factors associated with outcome of the patients who needed liver transplantation.

Limitations

Our study has several limitations. This is a retrospective analysis of cases despite the organized prospective data compilation. Because there are no particular descriptions of mushroom type by patients or relatives, and we did not determine the type of mushroom in our laboratory, this uncertain information make some biases in admitted cases. When symptoms happened after consumption of mushrooms, foodborne illnesses caused by other ingredients of the meal could not be eliminated. We did not include treatment parameters into the study that may play an important role in outcomes. Because we have no data on previous treatment of transferred patients (the majority of our cases), we could not include these data in our analyses. We did not evaluate the relationship of vital signs to outcome because we previously showed that vitals signs are not a parameter for outcome in MP. Unfortunately, we could not process the data concerning symptom time after ingestion, which is a parameter related to outcome. Finally, we could not use 16% of the data, which may affect the results. We also applied logistic regression analysis for age, presenting season, the means of obtaining mushrooms, and presenting symptoms. However, the group of variables that we chose here were not able to predict mortality and complication rate in high percentage of patients. The retrospective data collection and institution specific decisions on admissions and other critical factors related to patient management might have affected these results. Prospective data collection and choosing the variables after correlation with outcome measures will give a more accurate analysis on logistic regression.
Conclusion

We retrospectively analyzed demographic and clinical factors to evaluate their importance on outcome. Some factors, such as being elderly, summer season, purchased WM, and gastrointestinal symptoms, were significantly associated with mortality and complications in our study. Since our study showed that elderly patients have the highest mortality and complication rates, we suggest that emergency physicians and ICU physicians should pay special attention in taking care of this age group. Local or national laws should ban selling of WMs in public markets. Emergency physicians may also play a more active role in educating the public on MP. Since the mortality and complication rates of patients who directly presented to our tertiary care center was lower, we may suggest that MP cases should be transferred as soon as possible to experienced centers in high-risk regions. These variables and outcome measures should be evaluated and analyzed with logistic regression in prospective studies.

Acknowledgement

We are pleased to have Dr. Setenay Oner’s help with statistical analyses and Dr. Baran Tokar’s help with general evaluation of the manuscript.

Conflict of Interest

The authors declare that there is no potential conflicts of interest.

Financial Disclosure

This research received no specific grants from any funding agency in the public, commercial, or not-for-profit sectors.

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