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ORIGINAL ARTICLE

Prediction of the Development of Acute Liver Injury in Mushroom Poisoning by Hemogram Parameters

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Abstract

Introduction: Predicting acute liver damage caused by mushroom poisoning from hemogram parameters at first admission to hospital.

Methods: This retrospective study involved adults ≥18 years old who presented to the emergency room with mushroom poisoning from January 2011 to January 2017. Diagnosis of mushroom poisoning was made by a recent history of eating mushrooms, the onset of gastrointestinal symptoms such as diarrhea, vomiting, or abdominal pain after eating mushrooms, and excluding other possible causes of acute liver damage. Acute liver injury was defined as a 5-fold or greater increase in liver enzymes or the development of moderate coagulopathy (international normalized ratio > 2.0). First admission hemogram parameters of those who had liver damage and those who did not develop liver damage in the emergency department were compared.

Results: Acute liver injury developed in ten of 136 patients (68 women (50%), 68 men (50%), and mean age 39.5 years) included in the study. Three of them died (in-hospital mortality – 30% and mushroom poisoning overall mortality – 2.2%). Among the hemogram parameters, hemoglobin (13.9±1.7 g/dL vs. 15.4±1.7 g/dL, p=0.013), mean platelet volume (MPV) (7.6±1.02 fl versus 8.8±1.1 fl, p<0.05), and red cell distribution width (RDW) (16.5±4.8% vs 24.3±13.7%, p=0.034) in those who developed acute liver injury were significantly higher than those that did not develop.

Discussion and Conclusion: The high levels of MPV and RDW in the hemogram examination of the patients presented to the emergency department with mushroom poisoning may help to predict the progression of acute liver injury.

Keywords: Injury; liver; mushrooms; poisoning.

Mushroom poisoning is a common and important public health problem all over the world. Despite many research on this subject, it cannot be said that there is a definite and effective way in diagnosis and treatment. Examination and laboratory findings of most of the patients who are admitted to the hospital with complaints of poisoning after eating mushrooms are not specific. However, patients should be hospitalized and treated. Clinical and biochemical follow-up is needed as acute liver damage and death may occur. It cannot clearly be predicted in which patients will develop acute liver damage or die. It is known that timely liver transplantation is life-saving in appropri-

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ate cases[1]. Some scoring systems are available to identify patients who need liver transplantation in acute liver failure. However, there is no clear scoring system in liver failure stems from mushroom poisoning[1]. Basic complete blood count test is performed for every patient who is admitted to the emergency department with the complaint of mushroom poisoning. This study was conducted to identify easy to apply inexpensive markers that can be used for early prediction of the development of acute liver damage in cases with mushroom poisoning and to take necessary precautions.

Materials and Methods

Study Design and Data Collection

This retrospective study was conducted in a single center, in the University of Health Sciences Turkey, Haydarpaşa Numune Health Training and Research Hospital, Istanbul. The files of related patients over the age of 18, who were admitted to the emergency department and hospitalized in the internal medicine service between January 2011 and January 2017, were examined through the system. Diagnosis of mushroom poisoning was made by checking the recent history of eating mushrooms, the onset of gastrointestinal symptoms such as diarrhea, vomiting, or abdominal pain after eating mushrooms, but other possible causes of acute liver damage were excluded from the study. Acute liver injury was defined as a 5-fold or greater increase in liver enzymes or the development of moderate coagulopathy (international normalized ratio [INR]> 2.0). All hemogram parameters of those who had liver damage and those who did not develop liver damage in the emergency department were compared. The study was initiated after the approval of the Ethics Committee with the decision number HNEAH KAEK 2017/33.

Statistical Analysis Methods

Descriptive statistics were used to define continuous variables (mean, standard deviation, minimum, median, and maximum). To make a comparison of independent and normally distributed two continuous variables, Student's t test and Mann–Whitney U-test were used to compare two independent variables that do not conform to normal distribution. Chi-square or Fisher's exact test where appropriate was used to examine the relationship between categorical variables. The statistical significance level was set at 0.05. Analyses were performed using MedCalc Statistical Software version 12.7.7 (MedCalc Software bvba, Ostend, Belgium) Program.

Results

Of the 136 patients included in the study, 68 were female (50%) and 68 were male (50%). The average age of the patients was found to be 39.5 years. Acute liver injury developed in ten of the patients (7.4%). Three of them died (3/10 in-hospital mortality 30%). Overall, mortality due to the mushroom poisoning was found to be 2.2% (3/136).

Five of the patients who developed acute liver injury were male and five were female. Their average age was 39.4 years.

In Table, a comparison of the first acute liver damage blood test results which were obtained at the application of the patients to the emergency department was made.

Among the hemogram parameters, hemoglobin, mean platelet volume (MPV), and red cell distribution width were significantly higher among those who developed acute liver injury than those who did not (Table 1).

From biochemical parameters; alanine aminotransferase (ALT), aspartate aminotransferase (AST), and total bilirubin were significantly higher in those who developed acute liver injury than those who did not develop (Table 1).

However, white blood cell, platelet counts, blood urea nitrogen (BUN), creatinine, and prothrombin time (PT) – INR values were not significantly different in patients with and without acute liver injury (Table 1).

Table 1. Comparison of initial blood test findings according to the development of acute liver injury

	Acut Liver Injury		p
	Not Developed Mean±SD	Developed Mean±SD	
WBC (10^3/μL)	11337.4±4317.3	12102±3760.9	0.445
Neutrophil (10^3/μL)	8539.8±4227.7	9304±3485.3	0.357
Lymphocyte (10^3/μL)	1963±1061.8	1947±721.2	1.00
Hemoglobin (gr/dL)	13.9±1.7	15.4±1.7	0.013
Hematocrit (%)	41.6±4.8	45.5±5.5	0.056
MCV (fL)	87.4±5.6	87.9±5.6	0.626
MPV (fL)	7.6±1.02	8.8±1.1	<0.05
RDW (%)	16.5±4.8	24.3±13.7	0.034
Platelet (10^6/μL)	234146.8±68363.6	245100±94955.5	0.835
BUN (mg/dl)	15.3±5.7	17.7±10.4	0.828
Creatinine (mg/dL)	0.8±0.3	1±0.4	0.140
ALT (U/L)	31.5±41.3	139.9±142.7	<0.001
AST(U/L)	25.7±20.6	128±123.7	<0.001
INR	1.04±0.1	2.08±3.4	0.831
Total Bilirubin (mg/dL)	0.78±0.6	1.6±1.8	0.049
Direct Bilirubin (mg/dL)	0.3±0.1	0.47±0.4	0.036

Discussion

Although mushroom poisoning is a common health problem all over the world, the clinical symptoms are not frequently specific in poisoning. The genus of the fungus that causes the poisoning cannot be determined and if there is no anamnesis in a patient with signs of gastroenteritis, mushroom poisoning is generally not suspected[2].

It is known that there are 3000–5000 species of mushrooms in the world. Of these, only 70–100 are toxic to humans[3]. Amanita phalloides is responsible for most of the deaths that occur with this toxic species[4]. Death in amatoxin poisoning usually stems from severe liver cell necrosis.

Mortality rates varying between 4.8% and 34.5% have been reported in mushroom poisoning[5]. In our study, the mortality rate was found to be 2.2% (3/136). Mortality was seen in 30% of the patients who developed acute liver damage (3/10).

Fungal acute liver injury is potentially fatal and the definitive treatment is liver transplantation[6]. Other studies showed that compared to the survivors, BUN, AST, ALT, lactate dehydrogenase, total bilirubin, and PT were significantly higher in patients who lost their lives[7].

The most difficult part of liver transplantation is to decide its timing. Acute liver damage can progress very quickly and most of the patients who have been decided for a transplant, fall into multiorgan failure while waiting for it[8]. It may be too late to act after the emergence of multiorgan insufficiency, cerebral edema, or renal failure. However, it may be too early to make a decision before these findings. Therefore, many studies have been conducted to develop criteria for liver transplantation[9]. However, there is no agreed guideline yet. Many groups accept the King's College Criteria (KCC). In cases of poisoning other than paracetamol in KCC: PT >100 sec, INR >6.7, or any three of the following should be existent; viral and non-drug etiology, the time between the onset of jaundice and encephalopathy being more than 7 days, being <10 years old or >40 years old, and having total bilirubin >17.4 mg/dL[10,11].

On the other hand, there are studies reporting that serum creatinine level has a higher prognostic value than bilirubin level, especially in amatoxin intoxications. In a study conducted in Germany by Ganzert et al.[12] (2005), to determine prognostic factors, 198 amatoxin intoxication cases were retrospectively analyzed and it was concluded that evaluating creatinine level and prothrombin index together is the most appropriate method in determining the prognosis. On the other hand, in their study, Escuide et al.[13] analyzed 27 Amanita phalloides cases retrospectively, KCC and Ganzert criteria were compared and it was concluded that KCC was statistically more successful in predicting prognosis according to Ganzert criteria.

In our study, in accordance with the literature, the ALT, AST, and bilirubin levels were found to be significantly higher in those who developed acute liver injury compared to those who did not. However, although BUN, creatinine, and PT values were found to be higher in those who developed acute liver damage than those who did not, they were not statistically significant. The reason for this is probably the low number of patients.

MPV is the most widely used measure of platelet size, a potential marker of platelet reactivity. Larger platelets are more metabolically and enzymatically active and have a greater prothrombotic potential. Studies show that higher MPV values are observed in diseases such as diabetes mellitus, hypertension, hypercholesterolemia, smoking, and obesity, and MPV may be an indicator of inflammatory processes[14-16].

Just like MPV, red cell distribution width (RDW) is one of the parameters in hemogram measurements, and it is a quantitative measurement of volume (size) changes in erythrocytes. Nowadays, RDW is also a recommended parameter to show inflammation. Regarding the use of blood level of RDW as a biomarker, there are studies conducted on renal failure, stroke, heart failure, and myocardial infarction[17,18]. Patel et al.[19] found that RDW values above 14 % are associated with high mortality regardless of the reason.

After the ingestion of toxic mushrooms, toxins cause initiation of inflammation, leading to damage and necrosis in hepatocytes. In our study on the basis of knowing that MPV and RDW levels are indicators of inflammatory processes, we found that compared to those who did not develop liver damage, patients with acute liver injury had significantly higher MPV and RDW levels at their first admission to the emergency department. These results emphasize that MPV and RDW can be used as a precursor of the development of acute liver failure and can be valuable for determining the need for further intervention such as liver transplantation.

When the liver enzymes of the patients with acute liver damage were increased, it was observed that the increase in MPV and RDW levels continued in the same way in the hemogram examinations.

Although the MPV and RDW values of the patients who died from mushroom poisoning were found to be high in our study, statistical evaluation could not be made due to the low number of patients who died (3/136). Studies with

higher patient numbers are needed for definitive results.

The purpose of our study is to obtain information about whether the development of acute liver injury is predictable from hemogram parameters, which are cheap, practical, and can be applied everywhere. In this way, it is aimed to identify patients with high mortality risk and be more aggressive in their treatment. Furthermore, predicting patients who may need treatments such as liver transplantation is another goal of this study. In this respect, we think that high MPV and RDW parameters may be a guide in predicting the course of liver failure in mushroom poisoning.

Limitations

There are several main limitations such as conducting this study in a single center, examining patient files retrospectively, and having no toxicological examination for any case. Multi-center studies in different populations are needed for more accurate results. It should also be kept in mind that undetected biases may be present.

Ethics Committee Approval: The study was initiated after the approval of the Ethics Committee with the decision number HNEAH KAEK 2017/33.

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Conflict of Interest: None declared.

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