

## RESEARCH ARTICLE

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## Mushroom Poisonings in Turkey: A Meta-Analysis Study

### ABSTRACT

**Objective:** The aim of this research is to examine the characteristics of mushroom poisoning (MP) seen in Turkey and to evaluate the results of clinical studies conducted on this subject in the last 20 years.

**Methods:** Google Scholar, PubMed, Science Direct and Scopus databases were scanned with the phrases "mushroom poisoning, mushroom poisoning in Turkey". 17 studies including sample volume, gender distribution, age average, complaint to the health institution, transplantation and full recovery rates were included in the analysis. In statistical data, random effects model was used.

**Results:** 17 different studies have been identified which give the average age of MP cases, nausea, vomiting, diarrhea and abdominal pain symptoms, liver and kidney failure, complete recovery and transplantation rates. The average age in studies involving MP cases was 38.2 years (95CI% 36.1-40.3). The average age determined as to whether the family members are adults, elderly or childhood is as expected.

**Conclusions:** Although the rates of admission to hospital according to gender distribution of MP patients are similar, the signs and symptoms at admission, the distribution of liver and kidney failure, and the rates of complete remission after transplantation vary significantly.

**Keywords:** Meta-Analysis, Mushroom Poisoning, Toxins.

## Türkiye'deki Mantar Zehirlenmeleri: Bir Meta-Analiz Çalışması

### ÖZET

**Amaç:** Bu araştırmanın amacı, Türkiye'de görülen mantar zehirlenmelerinin (MZ) özelliklerini incelemek ve son 20 yılda bu konuyla ilgili yapılan klinik çalışmaların sonuçlarını değerlendirmektir.

**Gereç ve Yöntem:** Google Scholar, PubMed, Science Direct ve Scopus veri tabanları "mantar zehirlenmesi, Türkiye'de mantar zehirlenmesi" ibareleri ile tarandı. Örneklem hacmi, cinsiyet dağılımı, yaş ortalaması, sağlık kuruluşuna başvuru şikayeti, transplantasyon ve tam iyileşme oranlarını içeren 17 çalışma analize dahil edildi. İstatistiksel verilerde rastgele etkiler modeli kullanılmıştır.

**Bulgular:** MZ vakalarının ortalama yaşını, bulantı, kusma, ishal ve karın ağrısı semptomlarını, karaciğer ve böbrek yetmezliğini, tam iyileşme ve transplantasyon oranlarını veren 17 farklı çalışma tespit edilmiştir. MZ olgularını içeren çalışmalarda ortalama yaş 38.2'dir (%95CI %36.1-40.3). Aile bireylerinin çocuk, yetişkin ya da yaşlı olup olmamasına göre belirlenen yaş ortalaması beklendiği gibidir.

**Sonuç:** MZ hastalarının cinsiyet dağılımına göre hastaneye başvuru oranları benzer olsa da, başvuru sırasındaki belirti ve bulgular, karaciğer ve böbrek yetmezliği dağılımları ve transplantasyon sonrası tam remisyona oranları önemli ölçüde değişmektedir.

**Anahtar Kelimeler:** Mantar Zehirlenmesi, Meta-Analiz, Toksinler.

## INTRODUCTION

Mushroom poisoning (MP) is an important life-threatening health problem with the potential to affect blood values (1). Depending on the variety of mushrooms consumed, a wide variety of clinical symptoms may occur (2). There are approximately 5000 poisonous mushroom species in the world and especially around 100 fungal species are responsible for most of the poisonings (3). Although the clinical picture that occurs in patients mostly complain of gastrointestinal system, in some cases, liver, kidney and nervous system damage and even death may be encountered. MP should be considered as a medical emergency from the first diagnosis and treatment should be applied quickly for a successful treatment result (4).

Fungi are examined in two categories as poisonous and nonpoisonous mushrooms (5). Cultured mushrooms are a non-poisonous (toxin-free) mushroom that grows under special conditions. The improper storage conditions of the cultivated mushroom and keeping it at an inappropriate temperature causes the growth of microorganisms. As a result, a gastroenteritis tabloid appears (6). The main poisonous toxins are; amanitis, ibotenic acid, giromitrin, muscimol, orellanin, psilosibin, muscarin and coprin (7).

Collecting and consuming wild mushrooms is a historical tradition in many European countries (8). A significant portion of the population in Turkey live in rural areas and are benefiting from some of the plants growing in the environment for various reasons. Consumption of poisonous ones, especially of these products consumed as food and medicine, causes poisoning. Although it varies very widely consumed in Turkey according to the types of wild mushrooms. However, mushroom pickers generally do not have sufficient information to distinguish poisonous mushrooms from non-toxic ones (9). Amanita mushroom poisonings are frequent in Turkey. Amatoxins ( $\alpha$ -amanitis and  $\beta$ -amanitis) produced by Amanita phalloides cause severe liver, kidney and central nervous system damage. Amanita phalloides has been reported to be responsible for 90% of fatal cases (10,11). The lack of a comprehensive meta-analysis about mushroom poisoning in Turkey in the literature directed us to this research.

The main aim of this research is to examine the characteristics of MP in Turkey in the last 20 years and evaluate the clinical results of MP.

## MATERIAL AND METHODS

Since our study will examine mushroom poisonings in our country, research results related to mushroom poisoning between 1999-2019 were needed. To this end, Google Scholar, PubMed, Science Direct and Scopus databases were scanned with the phrases "mushroom poisoning, mushroom poisoning in Turkey" and article results analyzed studies conducted in Turkey were evaluated. The references of the articles and abstracts were also

searched. The data in the articles included in the study were recorded on the SPSS program, no additional form was used for the data.

### Compliance Criteria of the Studies:

Original research papers that analyzed the cases of mushroom poisoning in Turkey were included in the study. The necessity of the studies to be included in the meta-analysis to have common parameters and statistical data for analysis was determined as the inclusion criteria in the years we investigated (12). The following parameters were included in our study: Giving the average age of MP cases, evaluating the symptoms of nausea, vomiting, diarrhea and abdominal pain, determining the rates of liver and kidney failure, complete with recovery or transplantation. Our limitation when researching studies was publication date and country. Native or refugee status was not used when examining studies. Scanned in Turkish and English. We didn't collect unpublished data.

**Selection and Data Extraction:** All the sources of information were searched by three authors (I.U., E.F.O.P. and H.B.). After the copies, titles and abstracts were removed, the full texts of the studies were scanned for the eligibility criteria. The appropriate study was included in the analysis after being evaluated by both researchers. A study that was deemed unsuitable for inclusion by one researcher was also evaluated by two other researchers. It was defined as a study not suitable for practice that did not meet the inclusion criteria. The study, which was determined as inappropriate by two researchers or led to disagreement between the three researchers for any reasons, was evaluated by the other researcher (E.C.). After than it was determined appropriate or inappropriate to be excluded from the analysis.

One of the two separate studies by Cevik AA et al. was published in 2007 and poisoning severity scores were evaluated. In their other study published in 2014, Cevik AA and colleagues examined the mortality and complication rates of mushroom poisoning cases that came to their clinics in the last 20 years. Studies have not been combined. Other than, there was no combinable studies.

**Analysis of Data:** In our study we have taken into consideration studies which evaluated the MP in Turkey. We planned to determine which complaints the poisonings apply to the health institution, the rates of organ failure, full recovery or transplantation. Each parameter determined for meta-analysis needs to be extracted and adjusted from the data obtained. For this reason, while we included those who have common parameters from 36 studies scanned from databases, we had to exclude other studies from analysis. While 17 studies including sample volume, gender distribution, age average, complaint to the health institution, transplantation and full recovery rates

were included in the analysis, 19 studies have common parameters according to the sample characteristics adapted to meta-analytical statistics in acceptable criteria since all or some of these values are not specified. They were excluded from the analysis.

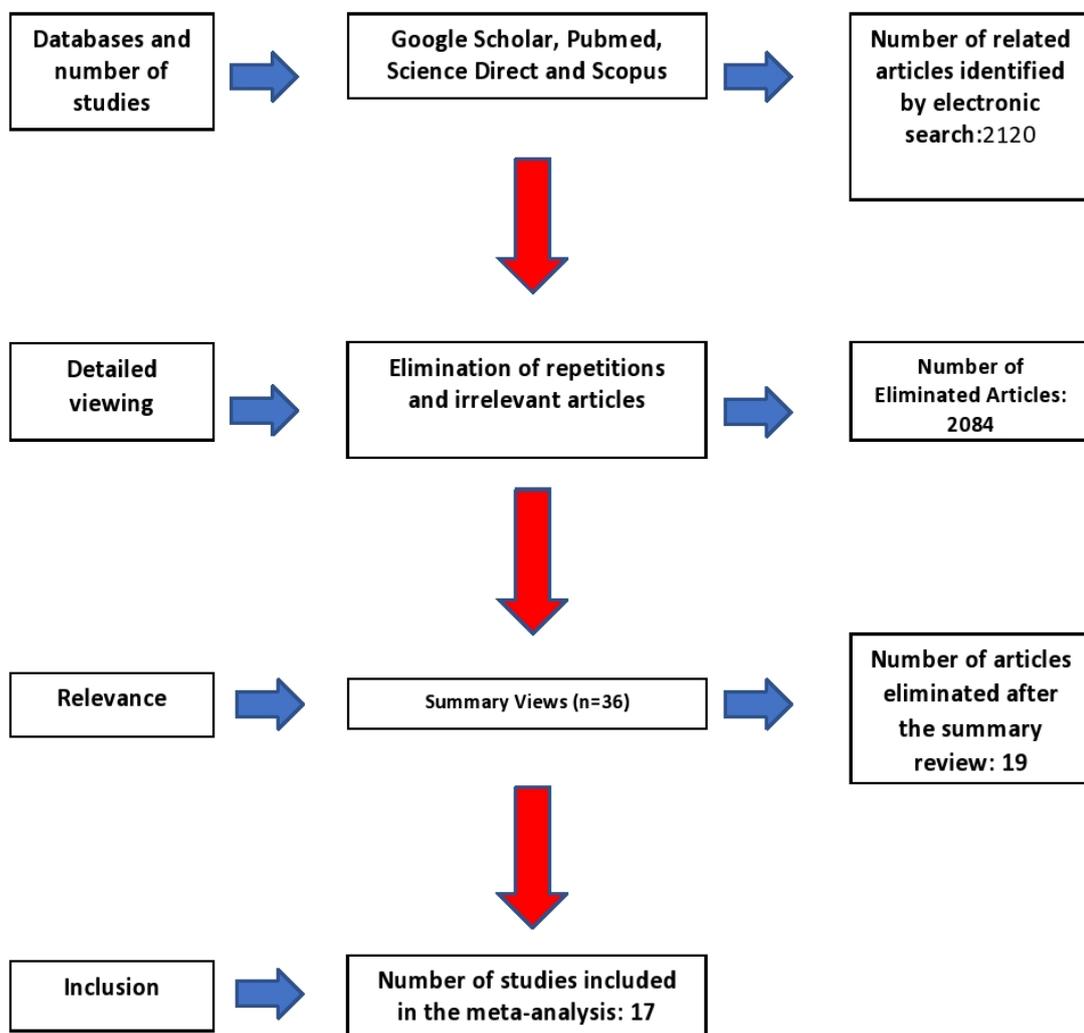
A statistical model should be chosen for meta analysis (13). If all studies are similar, a fixed-effect model will be appropriate. If the studies are changing in ways that may affect the effect size, the random effects model will be appropriate in the analysis. For this reason, it has been deemed appropriate to use the random effects model in this study. Model selection was determined based on the sampling frame, not on the result. Comprehensive Meta Analysis (CMA) Software Version (CMA V3, Biostat Inc, NJ, USA) was used for data synthesis. In statistical data, random effects model was used, standardized mean difference (SD) and 95% confidence interval (CI) were given in the analysis.

If the P value for Begg and Mazumdar Rank Correlation p value for Publication Bias is higher than 0.05, it indicates that there is no "publication bias". Begg and Mazumdar p values were

calculated for all analyzes and added to the tables as the last column. Since all p values are greater than 0.05, there is no "publication bias" in this study.

## RESULTS

We scanned 2120 studies from databases by as a result of the electronic search with keywords. As a result of detailed examination, it was observed that 2084 studies were excluded from the scope of the research. By examining the summary information, 36 studies were included in the research. Detailed with inclusion criteria, 17 studies were included in the meta-analysis. 17 different studies have been identified suitable in our research (Figure 1). These studies includes the average age of MP cases, nausea, vomiting, diarrhea and abdominal pain symptoms statues, liver and kidney failure rates and complete with recovery and transplantation rates. The cities where mushroom poisoning studies are carried out are Bolu, Bursa, Denizli, Eskişehir, İstanbul, Karabük, Malatya and Sivas. The Black Sea and Thrace regions were determined as the regions where the studies were carried out.



**Figure 1.** Flow chart showing the selection of reviews.

Descriptive statistics of these studies for categorical independent variables are given in Table 1. Homogeneous distribution value according to the

effect model of the studies, average effect size and confidence intervals are given in Table 2 and Table 3.

**Table 1.** Average Values of Studies Containing Mushroom Poisoning Data According to Sample Volume, Provinces and Gender Distribution

Studies	Sample volume	City or region where the research was conducted	Gender distribution	
			Woman	Man
Ahishali (2012) <sup>14</sup>	77	İstanbul	46	31
Bilir (2006) <sup>15</sup>	23	Eskişehir	13	10
Cevik (2007) <sup>16</sup>	307	Eskişehir	172	135
Cevik (2014) <sup>17</sup>	599	Eskişehir	319	280
Colak (2015) <sup>18</sup>	58	İstanbul	37	21
Erdur (2007) <sup>19</sup>	154	Denizli	77	77
Eren (2010) <sup>20</sup>	294	Sivas	173	121
Kavalci (2010) <sup>21</sup>	75	Trakya	40	35
Kiziltas (2013) <sup>22</sup>	84	İstanbul	52	32
Koksal (2013) <sup>23</sup>	53	Bursa	28	25
Koyuncu (2014) <sup>24</sup>	64	Karabük	32	32
Ozdemir (2004) <sup>25</sup>	26	Sivas	19	7
Petekmaya (2016) <sup>26</sup>	6	Malatya	2	4
Sonmez (2013) <sup>27</sup>	135	Other	90	45
Trabulus (2011) <sup>28</sup>	144	İstanbul	72	72
Yardan (2010) <sup>29</sup>	317	Karadeniz	214	103
Yilmaz (2015) <sup>30</sup>	648	Bolu	391	257

**Table 2.** Table of Homogeneous Distribution Value, Average Effect Size and Confidence Intervals in the Effect Models of the Studies Included in the Meta Analysis According to the Average Age

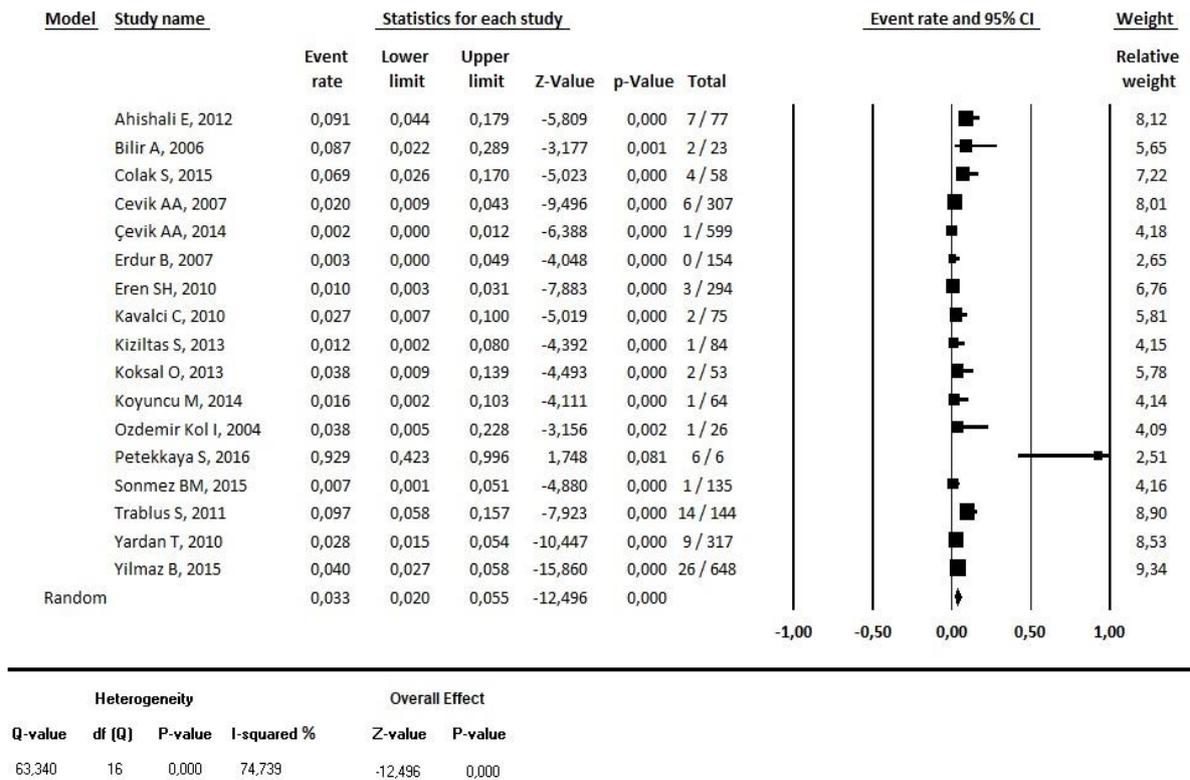
Model Type	n	Z	p	Q	Average Effect Size	For Impact Size 95% Confidence Interval		Begg and Mazumdar Rank Correlation p value for Publication Bias
						Lower Limit	Upper Limit	
Fixed	17	127.546	<0.001	181.926	37.380	36.806	37.955	0.537

**Table 3.** Table of homogeneous distribution value, average effect size and confidence intervals in the effect models of the studies included in the meta-analysis according to the complaint and symptom.

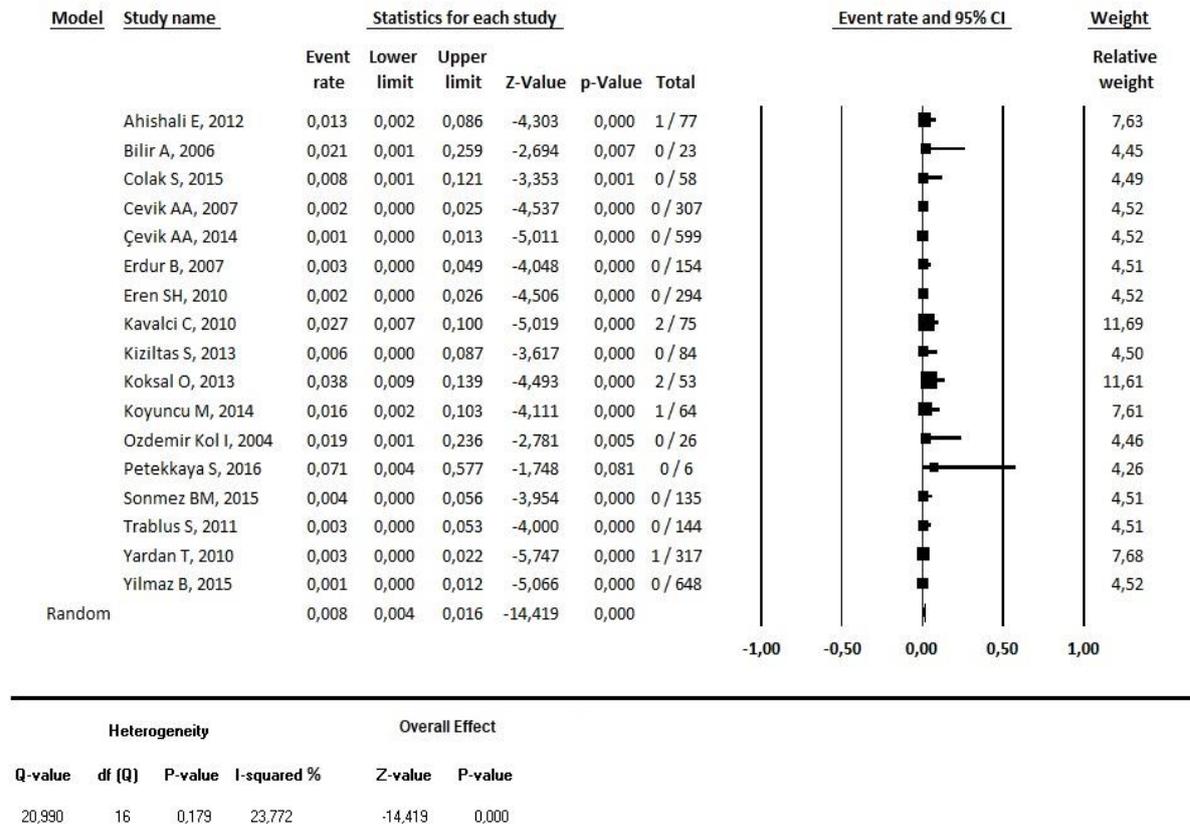
Complaint and Symptom	Model Type	n	Z	p	Q	Average Impact Size	For Impact Size 95% Confidence Interval		Begg and Mazumdar Rank Correlation p value for Publication Bias
							Lower Limit	Upper Limit	
Nausea	Fixed	17	6.389	<0.001	757.213	0.574	0.551	0.596	0.902
	Random	17	2.400	0.016		0.700	0.539	0.823	
Vomiting	Fixed	17	-0.672	0.502	1131.749	0.491	0.463	0.518	0.837
	Random	17	1.254	0.210		0.649	0.414	0.829	
Abdominal Pain	Fixed	17	-8.367	<0.001	474.044	0.414	0.394	0.434	0.202
	Random	17	-4.463	<0.001		0.244	0.165	0.347	
Diarrhea	Fixed	17	-13.045	<0.001	477.272	0.359	0.339	0.379	0.773
	Random	17	-5.058	<0.001		0.200	0.128	0.300	
Recovery	Fixed	17	29.269	<0.001	31.373	0.939	0.928	0.949	0.092
	Random	17	17.233	<0.001		0.950	0.932	0.964	
Acute Liver Failure	Fixed	17	-27.515	<0.001	63.340	0.042	0.034	0.051	0.711
	Random	17	-12.496	<0.001		0.033	0.020	0.055	
Acute Kidney Failure	Fixed	17	-24.073	<0.001	61.694	0.050	0.040	0.063	0.537
	Random	17	-11.594	<0.001		0.024	0.013	0.044	
Transplantation	Fixed	17	-16.579	<0.001	20.990	0.010	0.006	0.016	0.232
	Random	17	-14.419	<0.001		0.008	0.004	0.016	

The effect size and confidence intervals of the studies included in the meta-analysis according to the condition of acute liver failure,

transplantation statuses and the average effect size chart according to the Random Effects Model are given in Figure 2 and Figure 3.



**Figure 2.** The effect size and confidence intervals of the studies included in the meta-analysis according to the condition of acute liver failure and the average effect size chart according to the Random Effects Model.



**Figure 3.** The effect size and confidence intervals of the studies included in the meta-analysis according to the transplantation status and the average effect size chart according to the Random Effects Model.

## DISCUSSION

Poisoning is a common cause of applying to the emergency room by patients. According to data from European hospitals, about 1% of all emergency room entries are related to poisoning. Although this is not seen as a very high rate at first glance, it becomes an important health problem considering the potential risk of death in most cases (14,15). For this reason, our systematic meta-analysis study's purposes are examine the distribution of poisoning in Turkey and the symptoms and what the findings to the relevant period together by setting transplantation rates with the cure rates and organ failure cases about MP.

The quality of the conclusions and generalizations to be drawn from a meta-analysis depends on how the studies included in the meta-analysis are presented (16). At the same time, one of the biggest difficulties in meta-analysis studies is that printed publications are considered suitable for printing if they have a strong effect or statistically significant (17). The absence of a strong impact or statistical significance of the studies carried out causes them to be deemed unsuitable to print. This prevents the homogenous distribution in the studies included in the analysis.

Seventeen studies were included in our study because they had the criterias(18-34). In all of these studies in which mushroom poisoning cases were evaluated; the average age of the sample, gender distribution, nausea, vomiting, abdominal pain and diarrhea symptoms, and the rates of referral to health institutions, liver and kidney failure, and transplantation and complete recovery rates are specified. Mushroom poisoning often causes a picture of gastroenteritis. Hepatotoxicity is associated with a limited group of fungi. Kidney failure; may be due to severe dehydration or specific toxin damage. Early syndromes (nausea and vomiting within 6 hours) are generally associated with a good prognosis, while delayed syndromes carry the risk of liver and kidney failure (35). In the studies included in the analysis, the rates of nausea and vomiting were higher than the random effects model among the complaints of applicants, compared to the rates of abdominal pain and diarrhea. While almost all of the studies included in the analysis were found to have liver and kidney failure in MP cases, in one study (23) they stated that they did not find the organ failure table in the cases they investigated.

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Especially after rainy weather, a wide variety of wild mushrooms grow spontaneously in forest areas and often leads to potentially fatal consequences by being consumed by local communities (36). Although it is known that fungi grow mostly after rainy weather, most of the studies included in the meta-analysis reported that MP cases were observed in the autumn season. In three studies in summer (20,24,29), in one study in spring (21) and in one study in winter (28) MP cases were reported more frequently.

Located in the traditional culture dishes in Turkey is carried out with public participation in the household. With the family elders, all adults and children in the house are replaced at the table (37). For this reason, it will be meaningful to evaluate the food cultures in the regions where the study is performed. As a result of the analysis, the average age in studies involving MP cases was 38.2 years (95CI% 36.1-40.3). The average age determined as to whether the family members are adults, elderly or childhood is as expected.

**Limitations:** There are many limitations on meta-analysis studies and integrity on the subject. We tried to make an extensive electronic search for this study, but some studies may have been missed during the searches. In addition, the studies were conducted on the pediatric and adult population, and we conducted our analysis without categorizing them by age group. We are of the opinion that evaluating studies in pediatric and adult populations in separate groups may be better in terms of elucidating the main approaches in MP cases.

As a result, a heterogeneous result set was encountered in our meta analysis as a result of the studies performed in different regions and with different sample volumes. Although patients vary in age and gender distribution of MP Turkey, symptoms and findings in admission to the hospital, liver and kidney failure distributions, and transplantation complete remission rates vary significantly.

Türkiye consists of various regions in terms of its natural structure and mushroom diversity is very high. For this reason, the clinical findings and results of mushroom poisoning cases seen in the regions are very diverse. In general, it is important to analyze mushroom poisoning cases in all cities and regions.

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