



Review article

Mortality rate and liver transplant in patients with mushroom poisoning: A systematic review & meta-analysis

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ABSTRACT

Background: Mushroom poisoning is raised as a poor food problem that can cause the death of patients or the need for a liver transplant.

Objective: This study was conducted with the aim of assessment the mortality rate and liver transplantation in people suffering from mushroom poisoning through a systematic review and meta-analysis.

Method: The study is designed and conducted based on the PRISMA statement. International databases have been checked for articles up to March 1, 2022. The results of the study are presented with the guidance of Garrard's statement. CMA software was used in meta-analysis.

Results: Thirty-three articles were selected for this study. The mortality rate reported 0–40% and the results of the meta-analysis showed that the mortality rate was 2.87%. in other hand the mortality rate was 1.4% with studies that reported zero death. Overall, 16 patients had liver transplants, that only 2 died after liver transplants and 14 others survived.

Conclusion: The death in patients with mushroom poisoning is significant. Patients with liver disorders and patients or kidney disorders are more likely to have a poor prognosis. Liver transplant can be lifesaving. Also, quick referral of patients in the early stages reduces the need for liver transplantation.

1. Introduction

Food poisoning includes a large group of acute and sometimes fatal prognosis events [1]. One of the causes of food poisoning is the use of poisonous plants and mushrooms [2,3]. In societies, poisoning caused by the consumption of plants and fungi is one of the most important and common issues in clinical toxicology [4]. Not only the nutritional role of plants and mushrooms is very important, but also the main basis of many drugs are plants and herbal products, so one of the problems of clinical toxicologists is cases of poisoning with these products [5,6]. Mushroom poisoning occurs in various developed and in developing countries, so this problem can be

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considered as a global problem [7–9]. It is estimated that out of 100,000 species of mushrooms worldwide, more than 100 species are poisonous [10]. The prevalence of mushroom poisoning is varying in different regions [5,6,11–13]. Usually, people with less knowledge about the type of mushrooms and in spring and autumn are more prone to poisoning than others, which can be very dangerous [5]. On the other hand, the type of fungus and toxins also affects the poor prognosis of poisoning [14,15], but what they need to pay attention to is that in 95% of cases, the type of fungus and toxins is not known, so diagnosis and treatment are based on the clinical symptoms in time of hospitalization [12,16]. Toxic mushrooms poisoning causes a wide range of symptoms in patients and ranges from mild gastrointestinal symptoms to organ failure and death depending on the type of fungus [13,17]. The most commonly reported symptoms are related to gastrointestinal symptoms, and also, the neuro-muscular disorders make a wide range of onset symptoms [18,19]. Acute kidney failure, acute liver failure, rhabdomyolysis, hemolysis, gastroenteritis, neuropsychiatric disorder and dermatitis are clinical syndromes caused with mushroom poisoning [11,12,20–22]. In addition, the presence of risk factors such as diseases of the gastrointestinal tract and liver, alcohol use and coagulation disorders, and diseases of the kidney system can affect the severity of symptoms and poor prognosis of MP [23]. Because of the lack of effective antidotes in this group of poisonings, treatments usually include care support and symptom management including gastric washing, active charcoal, hydration, high doses of penicillin G and *N*-acetylcysteine, and in cases of severe liver failure, is the liver transplant (LT) (MP2). overall, studies have shown that in case of poisonous mushroom consumption, the mortality rate of the poisoned person is expected to be up to 20% [11]. Due to the fact that a systematic review and meta-analysis study on the mortality rate and liver transplantation of mushroom poisoning has not been conducted so far, so this study was conducted with the mentioned purpose.

2. Method

2.1. Protocol and purpose

The aim of this study was to determine the mortality rate due to mushroom poisoning worldwide and liver transplantation. The protocol of this study has been approved by the Center for Systematic Review and Meta-Analysis of Kermanshah University of Medical Sciences with an approval/ethical code of IR. KUMS.REC.1400.341. This study was designed and implemented based on the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement [24,25].

2.2. Search strategy

In this study, we used PRISMA's statement in strategy design, search, study selection, and data extraction. A comprehensive search was conducted to find all articles by March 1, 2022 in international databases. The databases searched included Web of Sciences, PubMed, Scopus, and Google Scholar. We expanded the search strategy by using keywords related to the purpose of the study and keywords extracted from previous studies. Keywords were standardized using the Mesh term. Keywords used include a combination of words based on the search method in the database and include mushroom, fungus, poisoning, poison, death, mortality, prognosis, and liver transplantation, outcome. We searched the words in combine together in advanced searches in database and with use of commands (such as AND, OR). In addition, we searched the references of other articles for similar studies.

2.3. Inclusion and exclusion criteria

All articles were included in the study until March 1, 2022. We included articles with observational design and excluded other articles such as reviews, meta-analysis, letters, commentary and similar articles. In articles that reported more than one data, we extracted and reported all the information.

2.4. Search validity and selection of studies

The search and selection steps of the studies have been designed and implemented with the guidance of PRISMA Statement and similar reviews [25–27]. All searched studies using different keywords, were entered into Endnote V.20 software for review. Duplicate titles were removed in the software. The remaining titles were then checked by two of the research team members (MJ, MJ) to remove unrelated titles. Then, the type of design and abstract of the remaining articles were screened and then articles with the wanted design and information, entered to the next step. finally, the full text of the remaining papers was carefully screened several times by the research team and the articles with the desired information were selected to extract the information. To extract the information, the full text of the remaining articles was examined in detail several times and the data was extracted. Any differences in the process of searching and selecting studies and extracting information were resolved through group discussion.

2.5. Meta-analysis and publication bias

We performed a meta-analysis study to evaluate the mortality rate in patients with mushroom poisoning. Meta-analysis was performed using CMA software V.3. Due to high heterogeneity ($I^2 = 97.501$, $P = 0.000$) we used random effects for meta-analysis. We also investigated and reported publication bias using Egger Test and Funnel plot.

2.6. Extract data and reports

After screening the full text of all articles with inclusion criteria, information was extracted and reported according to the purpose of the study. We used the Garrard statement 2020^{ed} to report data. The Garrard table is introduced by Judith Garrard and is a systematic way to report on systematic review and meta-analysis studies [28]. Reported information includes study characteristics (author, design, country, date of publication, duration of study), participants, outcome, liver transplantation, and mortality. In studies with more than one data, we reported all of the information.

3. Results

3.1. Search and included studies

1217 articles were found in the initial search. After removing duplicate titles, 712 papers were remained for further review. After reviewing the titles, 385 articles were removed due to unrelated titles and design contrary to the study criteria. Abstracts were then screened, leaving 50 articles for full-text review, and other articles were deleted for reasons such as lack of relevance to the purpose of the study, unrelated design, and insufficient information. In the full text screening phase, 33 articles were selected and their information was extracted and reported (Fig. 1).

3.2. Features of studies

Thirty-three articles were included in the study. These articles were published between 2010 and 2021 and the maximum length of

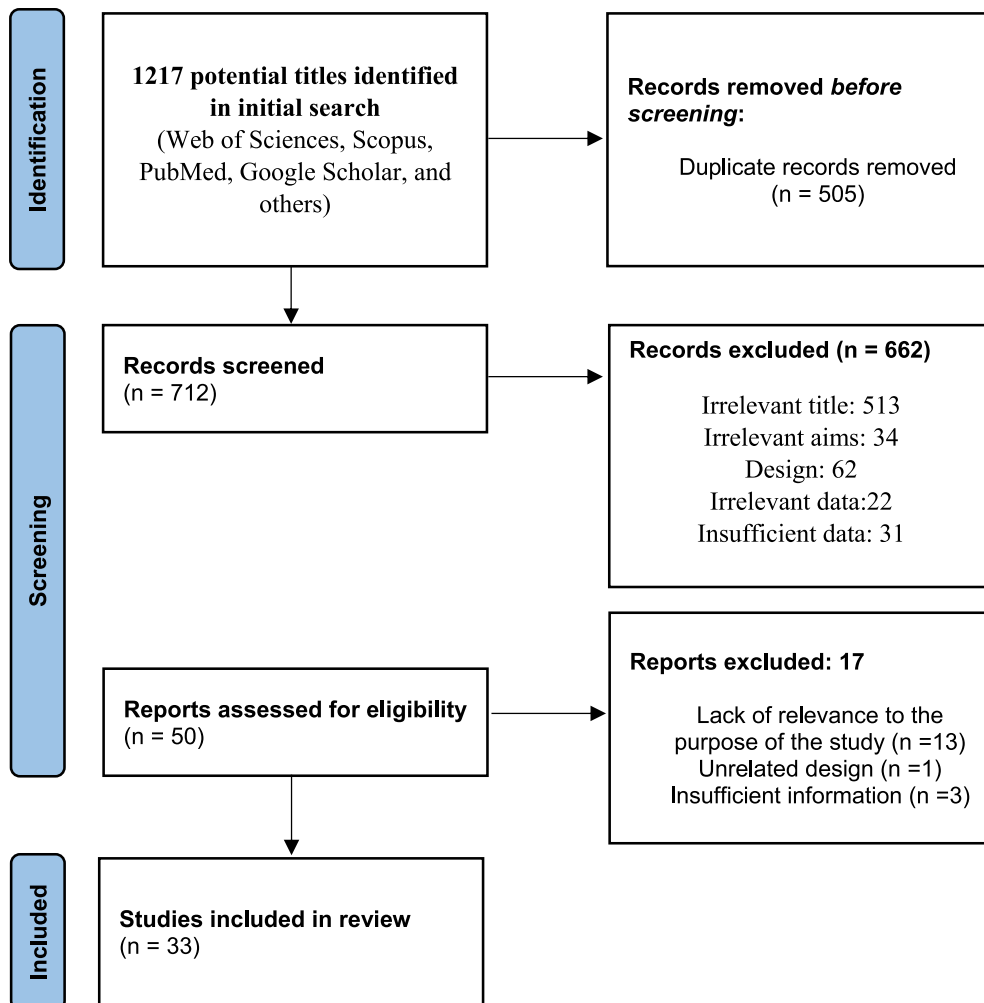


Fig. 1. Abstract of Study Selection and Findings (Based on the 2020 PRISMA statement [25]).

the study period was 30 years. In general, the length of the review period in the included articles was 284 years and 7 months in 12 countries. Most studies were conducted in the United States (7 articles) and then in China (6 articles). The frequency of patients with mushrooms poisoning in these 33 articles was 580677 patients. These 33 articles included information on patients' mortality rates. And 8 articles, including information on liver transplant patients (Table 1).

3.3. Liver transplant

In 8 articles, patients underwent liver transplantation. In total, 16 patients with mushroom poisoning underwent liver transplants, of which only 2 died after liver transplants and 14 others survived (Table 2).

3.4. Mortality rate

Mortality rates in patients with mushroom poisoning have been reported up to 40%, although in 13 articles, mortality was reported at 0% (Table 3). To examine the overall mortality rate, we considered all articles, which based on a meta-analysis of 33 articles, the mortality rate was 1.4% (Fig. 2). By deleting articles with a zero-mortality rate, the meta-analysis results showed that the mortality rate in the remaining 20 articles was 2.87% (Fig. 3). The results of Egger's test showed that there was no publication bias among the articles ($t = 0.153$, $P = 0.439$) (Fig. 4).

4. Discussion

Of these 33 reviewed studies, the most countries that conducted research on mushroom poisoning were the United States with 7 studies, China with 6 studies, and Iran with 5 studies. The highest study duration was 30 years in France, 21 years in Italy, and 18 years in America. Most of the studies were retrospective. The highest frequency of poisoned people was reported in Italy with 379,443 people, America with 133,700 people and China with 38,676 people. The success rate of liver transplant in poisoned patients was higher in USA, China and Czech countries respectively. The highest mortality rate in the studies was Australia 4 people (33.3%), Thailand 15 people (27.3%) and China 24 people (22.9%). The total frequency of mushroom poisoning patients was 580,677. The overall death rate of mushroom poisoning was 1.4%. A review study by Diazetal showed that most of the fatal poisonings of

Table 1
Included studies in review (n = 33).

Studies	Long of Study/pub date	Study design	Participants	Country
Jongthun et al. [23]	12 Ys/2020	CS	74	Thailand
Goli Khatir et al. [29]	4 Ys/2020	CS/Retro	65	Iran
Tawatsin et al. [13]	10 Ys/2018	CS/Retro	15,680	Thailand
Roberts et al. [30]	13 Ys/2013	CS/Retro	12	Australia
Li et al. [31]	1 Y/2020	CS/Retro	769	China
Chaudhary et al. [32]	1.5 Ys/2013	CS/Pros	60	Nepal
Silakhori et al. [8]	3 Ys/2018	CS	17	Iran
Bonacini et al. [33]	17 Ys/2017	CS/Retro	27	United States
Brandenburg et al. [5]	18 Ys/2018	CS/Retro	133700	United States
Trakulsrichai et al. [34]	3 Ys/2017	CS/Retro	55	Thailand
Cassidy et al. [35]	6 Ys/2011	CS/Retro	70	Ireland (UK)
Li et al. [22]	11 Ys/2021	CS	38676	China
Cervellin et al. [14]	21 Ys/2018	CS/Retro	379443	Italy
Eren et al. [36]	8 Ys/2010	CS/Retro	294	Turkey
Colak et al. [37]	3 Ys/2014	CS/Retro	58	Turkey
Keller et al. [38]	17 Ys/2018	CS/Retro	51	Switzerland
Chen et al. [39]	3 Ys/2021	CS/Retro	429	China
Gawlikowski et al. [40]	8 Ys/2014	CS/Retro	457	United States
Chan et al. [15]	10 Ys/2016	CS	67	Hong Kong
Soltaninejad [12]	1 M/2018	CS	1247	Iran
Badsar et al. [41]	5 Ys/2013	CS/Retro	102	Iran
Kieslichova et al. [42]	9 Ys/2018	CS/Retro	23	Czech
Vo et al. [43]	1 M/2017	CS	14	United States
Gold et al. [44]	3 Ys/2021	CS/Retro	556	United States
Dadpour et al. [45]	6 Ys/2017	CS	32	Iran
Kintziger et al. [46]	5 Ys/2011	CS/Retro	1538	United States
Saviuc et al. [47]	30 Ys/2010	CS/Retro	301	France
Schenk-Jaeger et al. [6]	15 Ys/2012	CS/Retro	6307	Switzerland
Schmutz et al. [48]	11 Ys/2018	CS/Retro	87	Swiss
Sun et al. [49]	1 Y/2018	CS	10	China
Moss et al. [50]	14 Ys/2018	CS/Retro	34	United States
Yardan et al. [51]	6 Ys/2010	CS/Retro	317	Turkey
Ye et al. [52]	10 Ys/2020	CS/Retro	105	China

Ys: Years, M: Month, CS: Cross sectional, Retro: Retrospective, Pros: Prospective.

Table 2
Studies in MP patients with liver transplantation (n = 8).

Studies	Patients With LT (of all)	LT outcome
Bonacini et al. [33]	1 (of 27)	Survived
Trakulsrichai et al. [34]	1 (of 55)	Died
Cervellin et al. [14]	1 (of 379443)	Survived
Chan et al. [15]	2 (of 67)	Survived
Kieslichova et al. [42]	6 (of 23)	1 Died/5 Survived
Vo et al. [43]	3 (of 14)	Survived
Schenk-Jaeger et al. [6]	1 (of 6307)	Survived
Yardan et al. [51]	1 (of 317)	Survived

Table 3
Mortality rate in reported studies (n = 33).

Studies	Participants	Mortality (%)
Jongthun et al. [23]	74	4 (5.4)
Goli Khatir et al. [29]	65	0
Tawatsin et al. [13]	15,680	79 (0.5)
Roberts et al. [30]	12	4 (33.3)
Li et al. [31]	769	22 (2.86)
Chaudhary et al. [32]	60	4 (6.6)
Silakhori et al. [8]	17	0
Bonacini et al. [33]	27	3 (11.1)
Brandenburg et al. [5]	133700	52 (0.03)
Trakulsrichai et al. [34]	55	15 (27.3)
Cassidy et al. [35]	70	0
Li et al. [22]	38676	778 (2)
Cervellin et al. [14]	379443	0
Eren et al. [36]	294	3 (1)
Colak et al. [37]	58	1 (1.7)
Keller et al. [38]	51	0
Chen et al. [39]	429	2 (0.4)
Gawlikowski et al. [40]	457	0
Chan et al. [15]	67	1 (1.5)
Soltaninejad [12]	1247	1.5%
Badsar et al. [41]	102	0
Kieslichova et al. [42]	23	2 (8.7)
Vo et al. [43]	14	0
Gold et al. [44]	556	0
Dadpour et al. [45]	32	7 (22)
Kintziger et al. [46]	1538	0
Saviuc et al. [47]	301	0
Schenk-Jaeger et al. [6]	6307	1 (0.015)
Schmutz et al. [48]	87	0
Sun et al. [49]	10	4 (40)
Moss et al. [50]	34	0
Yardan et al. [51]	317	3 (0.95)
Ye et al. [52]	105	24 (22.9)

mushrooms containing amatoxin lead to liver transplantation, and with liver transplantation in them, the survival rate increases [53]. In the study by Zhang et al. in China, out of 135 patients poisoned with mushrooms, 18 died, the mortality rate was reported as 11.8%. Sixty-one of the poisoned patients had liver damage and all of them recovered [54]. The study of Dadpour et al. (2017) in Iran showed on the 32 patients poisoned with mushrooms, 19 (59%) were discharged with full recovery, 7 (22%) died and 6 (19%) were leaved the hospital by personal consent. Mortality due to mushroom poisoning was reported to be 1.5%. There was no correlation between the mortality rate and the increase of liver transaminases and serum bilirubin, and the gastrointestinal problems were the most common consequence seen in those who were poisoned [45]. In the study by Keller et al. in Switzerland, zero mortality rate was reported and the most reported complications after mushroom consumption was digestive disorders [38]. Evidence from the studies of Çalişkanetal and Guleal in Turkey showed that the most common complication of MP was digestive problems. The most common laboratory finding was increased liver enzymes. And two of the patients had liver failure and underwent liver transplantation [55,56]. The results of another study in Iran that conducted by Silakhori et al. showed that the mortality rate of 17 patients poisoned with mushrooms was zero, and only one patient had elevated AST levels without evidence of liver failure [8]. In the study of Bonacini et al. in United States, reported that Amanita phalloides poison caused liver damage in 24 patients and Amanita ocreata poison in 3 patients, and 23 patients survived without liver transplantation and 4 patients had poor results. Among these poisoned people, one woman underwent a liver transplant 20 days after consuming mushrooms, and 3 women died due to liver failure [33]. In the study of Chen et al. in China, 429 cases of poisoning with poisonous mushrooms were reported, of which 2 people died and 84 people were hospitalized. The incidence of

Mortality Rate of Mushroom Poisoning

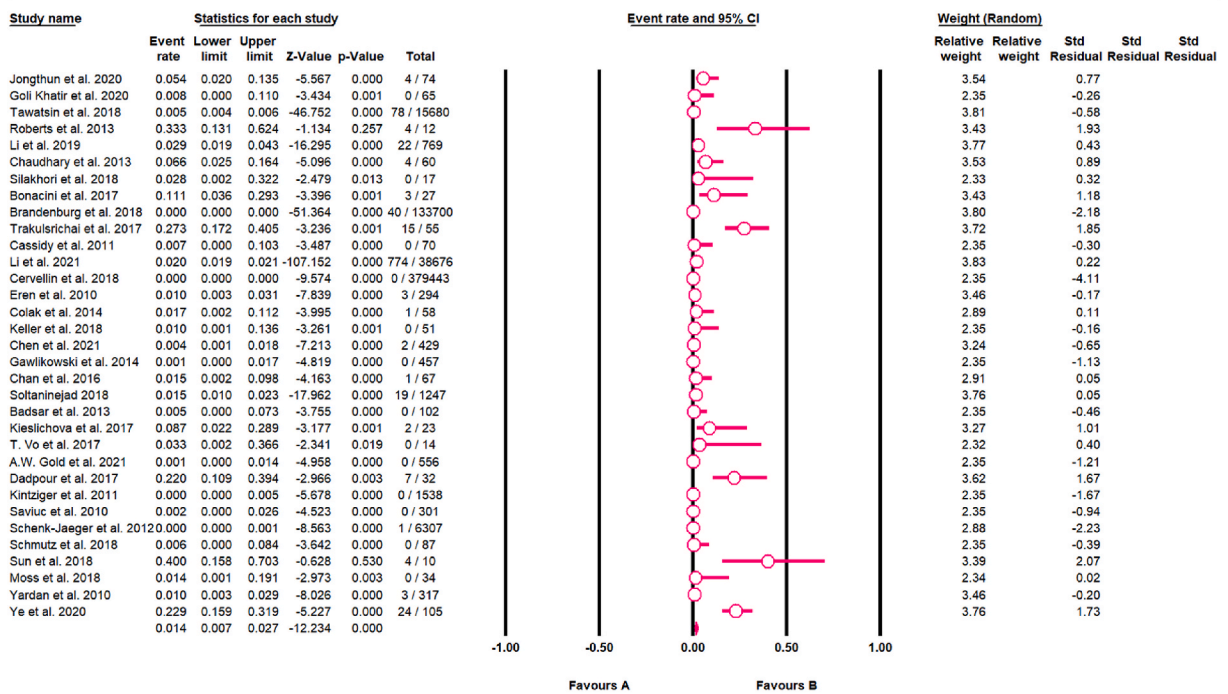


Fig. 2. The mortality rate of mushroom poisoning.

Mortality Rate of Mushroom Poisoning (without studies with 0 mortality)

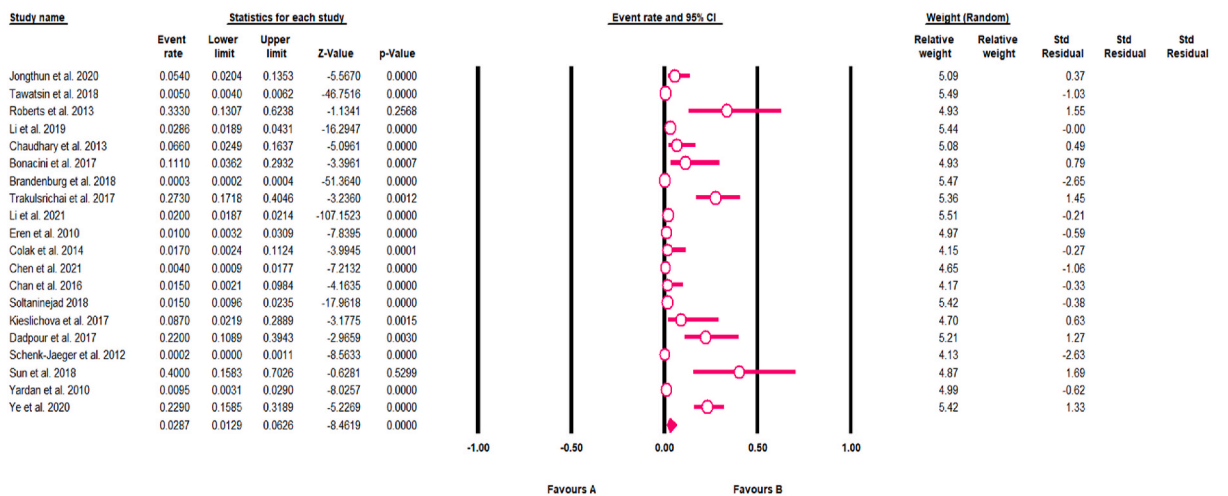


Fig. 3. Mortality rate without studies with zero death.

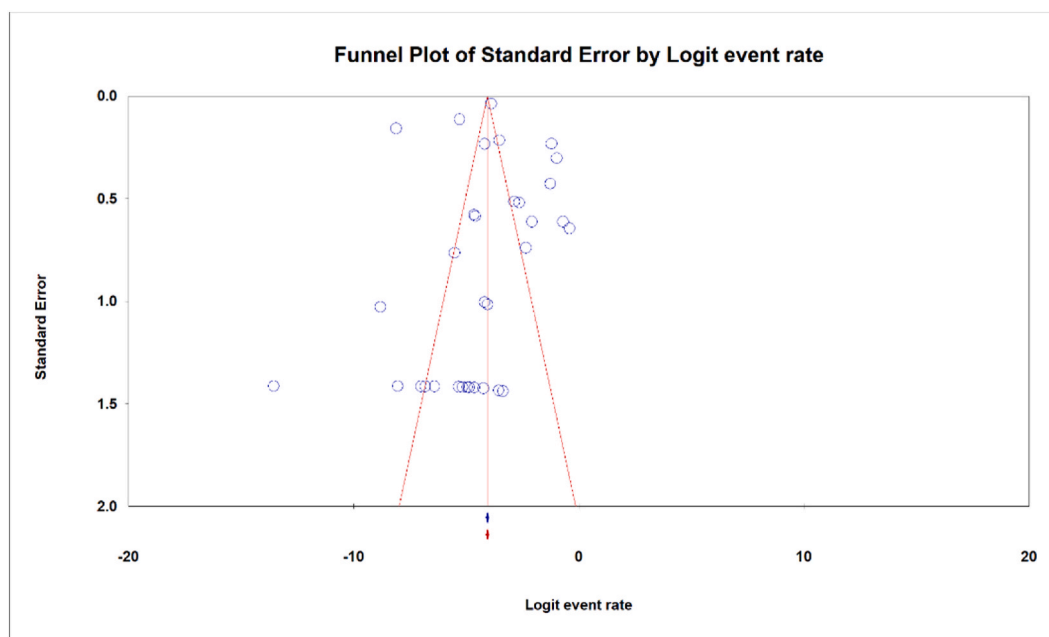


Fig. 4. Funnel plot for publication bias of included studies.

poisoning was 0.25 per 100,000 populations and the mortality rate was 0.47%. The most observed consequence in poisoned people was digestive problems [39]. Also, the study of Trakulsrichai et al. in Thailand showed that the mortality rate was 27.3%. Liver transplant was performed in one person, unfortunately, that person also died [34]. Evidence from Dutta's studies in India, respectively, showed that 13 of 94 mushroom-poisoned patients (13.8%) died, and 17 of 44 patients (38%) had liver failure. In 10 mushroom-poisoned patients with delayed liver failure, the mortality rate was 58%. Digestive, kidney and liver problems were among the common consequences of patients [57,58]. In a study conducted by Ostadtaghizadeh et al. in Iran, out of 1151 people poisoned by mushrooms, 1133 people (98.4%) were hospitalized and unfortunately 18 people (1.56%) died. Most of the patients presented with gastrointestinal symptoms, but died due to acute liver failure [59].

Poisoning is can incidence in both gender however it seems that male gender is more usual [60,61]. Baskiran et al. reported that the presence of encephalopathy, end-stage liver disease, INR, bilirubin, ammonium levels, and lower platelet count was related to poor prognosis in MP [62]. Elderly patients are more suffer from severe complications of mushroom poisoning than others and the death is more in this group, and also people that poisoned in summer suffer more severe complications [60]. The poisoning in summer is more reported. It has been reported that the death rate is higher in patients who bought poisonous mushrooms than those who harvested mushrooms themselves [22,60]. This can show the effect of the person's awareness on the type of mushroom harvests on the outcome of poisoning.

The results of numerous studies indicate that the death rate of patients with mushroom poisoning is significant, and liver complications are the biggest factor in their death. This consequence is so important that death has occurred even with liver transplantation. Therefore, rapid diagnosis of poisoning as an intervention solution to prevent acute liver failure seems necessary.

4.1. Implications

This paper is the first study in mortality rate of mushroom poisoning in systematic review or meta-analysis. We searched for all eligible studies and reported the mortality rate with to estimate. The discussion is focused on the approved and potential risk factors for incidence, poor prognosis, and liver transplant. The results of this study can be useful for further researches.

5. Conclusion

The results of this study showed that the liver transplantation is performed in few cases. The mortality rate was estimated 2.87% in studies with dead patients and was 1.4% in all studies. The most reported complications are liver disorders and also patients with history of liver disease or kidney disease are more likely to have weak prognosis.

Consent for publication

Not Applicable.

Availability of data and materials

This study is a review and the raw data are available in references studies.

Funding and financial disclosure

This study did not receive any financial support from any organization, or institute or personal financial interests.

Authors' contributions

Maryam Janatolmakan and Alireza Khatony contributed in concept of study. Maryam Janatolmakan, Milad Jalilian, and Alireza Abdi performed the comprehensive search and data extraction. The meta-analysis study conducted by Shahab Rezaeian and Milad Jalilian. The final report and manuscript were written, edited, and confirmed by Maryam Janatolmakan, Alireza Khatony, Milad Jalilian, Alireza Khatony, and Shahab Rezaeian.

Declaration of competing interest

The authors declare that they have no known competing financial or personal or other conflict of interest to declare.

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