Echinococcus granulosus, a parasite producing hydatid cyst: a review

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Abstract

Echinococcosis is a parasitic disease caused by tapeworms of the *Echinococcus genus*, such as *Echinococcosis granulosus*. The disease is characterized by the development of hydatid cysts, particularly in the liver and lungs. *Echinococcosis granulosus* has a complex life cycle involving dogs as definitive hosts and herbivores like sheep as intermediate hosts. Humans are accidental hosts who can become infected by consuming contaminated food and water containing Echinococcus eggs. The hydatid cysts is prevalent in rural areas of Africa, the Mediterranean region, South America, Central Asia, and Eastern Europe, where close contact between humans, dogs, and livestock is common. Clinical symptoms of hydatid cysts may have no symptoms for years. However, as cysts grow, they can cause various symptoms, including abdominal pain, nausea and vomiting, chest pain, cough, headache, seizures and vision problems and shortness of breath. Effective treatment of hydatid cyst is through surgery and Chemotherapy.

Chemotherapy have adverse side effects, so plants are used for treatment because of less side effects and safer.

If left untreated, a hydatid cyst can lead to serious problems such as organ failure, rupture, and even death. Understanding the epidemiology, life cycle of *Echinococcosis granulosus* is crucial for improving diagnosis, treatment, and control measures. Therefore, the aim of this review is to study *Echinococcosis granulosus* to improve diagnosis, treatment, epidemiological understanding and prevention strategies to reduce the public health impact of cystic echinococcosis.

Keywords: definitive hosts, Echinococcus granulosus, hydatid cysts

Introduction

Hydatid cyst disease, also known as cystic echinococcosis, is common in several regions of the world (1). Cystic echinococcosis is a serious zoonotic disease caused by the larval stage of *Echinococcus granulosus*. *Echinococcus granulosus* has a life cycle with dogs as the definitive host and sheep, goats or other livestock as intermediate hosts (2).

Hydatid cyst disease is especially common in rural, underdeveloped areas where people raise livestock, such as

- Africa: Hydatid disease is a major public health concern in many African countries, including North Africa, the Horn of Africa, and Southern Africa. Countries with high incidence rates include Morocco, Tunisia, Algeria, Libya, Egypt, Ethiopia, Kenya, and South Africa (*3*).
- South America: Hydatid disease is endemic in several South American countries, especially Argentina, Peru, Chile, and Uruguay. The disease is associated with the domestic dog-sheep cycle in these regions (4).
- Mediterranean region: Hydatid disease is common in Mediterranean countries, including Spain, Italy, Greece, and Turkey (5).
- Central Asia: Hydatid disease is a significant problem in Central Asian countries like Kazakhstan, Kyrgyzstan, Tajikistan, Turkmenistan, and Uzbekistan (6).
- Eastern Europe: Hydatid disease is found in parts of Eastern Europe, such as Romania and Bulgaria (7).

The high incidence of hydatid disease in these regions is linked to the close contact between humans, dogs, and livestock, as well as poor sanitation and hygiene practices.

Hydatid cyst not only causes severe illness and possible death in humans, but also causes economic losses due to treatment costs and disability of patients as well as reduction of animal products.

The purpose of studying hydatid cyst and the Echinococcus parasite is to better understand and diagnose the parasitic disease cystic echinococcosis. This review will focus on hydatid cyst and hydatid cyst-producing parasite, diagnosis, transmission and epidemiology, and finally, prospects for treatment, control and prevention.

Echinococcus granulosus Parasite and Life Cycle

The parasite *Echinococcus granulosus* is a zoonotic tapeworm that primarily infects herbivorous animals such as sheep, goats, and cattle. The life cycle of *Echinococcus granulosus* involves a definitive host (dogs and other canids) and an intermediate host (sheep and other herbivores) (Fig1).

The adult tapeworm resides in the intestine of the definitive host, and the larval stages infect the intermediate host, developing into hydatid cysts in the liver and lungs (Fig2). *Echinococcus granulosus* eggs eventually enter the environment through the host's feces and can survive outside the host for up to two years. Eggs are ingested by intermediate hosts and larval stages develop in hydatid cysts. These cysts can grow slowly over several months and, if ingested by the definitive host, can develop into adult tapeworms and complete the life cycle (8).



Fig2. Hydatid cyst of the liver

Understanding the epidemiology, life cycle of *Echinococcus granulosus* is important for the following reasons:

1. Improving diagnosis and treatment: specific diagnostic tests and targeted treatment methods.

2. Implement transportation strategies: Identify high-risk areas and animal sanctuaries to implement effective management strategies.

3. Vaccine development: Identify protective antigens to design effective vaccines against human and animal hosts.

4. Drug resistance monitoring: Monitoring the emergence of drug-resistant strains to guide appropriate chemotherapy strategies.

5. Promoting One Health: Achieve integration between human, animal and environmental health, addressing this shared disease in humans and animals.

Therefore, The study of hydatid cysts and echinococcosis parasites is an important area of research to address the significant global burden of cystic echinococcosis.

The clinical symptoms and pathogen of hydatid cyst disease

Clinical symptoms of hydatid cyst disease depend on the location and size of the cysts. Many people with hydatid cysts may have no symptoms for years because the cysts grow slowly. However, as cysts grow, they can cause a variety of symptoms, including:

•Abdominal pain, nausea and vomiting (if there are cysts in the liver) (9)

•Chest pain, cough, shortness of breath (if there is a cyst in the lung) (9).

•Neurological symptoms such as headache, seizures and vision problems (if there are cysts in the brain).

• Allergy and anaphylaxis with cyst rupture (10).

If left untreated, a hydatid cyst can lead to serious problems such as organ failure, rupture, and even death. Early diagnosis and appropriate treatment, which may include a combination of surgery, medication and other interventions, are essential to control this viral disease(11, 12).

Prevention of hydatid cyst disease

Prevention of hydatid cyst disease involves disruption of the life cycle of *Echinococcus granulosus*. The main preventive measures are:

• Bathe the dog regularly with tapeworm medication to remove adult tapeworms from the intestines.

• Limit dogs' access to raw or infected livestock carcasses to avoid ingesting parasites (13).

• Dispose of contaminated animal parts by burning or deep burial.

• Educate people, especially in rural areas, about the importance of good hygiene, such as washing hands before eating and after handling animals.

• Improves sanitation and access to clean water in limited areas.

To implement monitoring and control program of hydatid disease in livestock (14).

Treatment of Hydatid Cyst Disease

Treatment of hydatid cyst disease involves various methods, each with its advantages and limitations. The choice of treatment depends on factors such as the size and location of the cyst, the patient's overall health, and the availability of medical resources.

Surgical Options

Surgical treatment is considered the most effective method for removing hydatid cysts. This involves radical surgery, where the entire cyst and surrounding tissue are removed, or conservative surgery, where only the affected organ is partially resected if possible (*15*).

Radical surgery is considered a better treatment method for hydatid cysts compared to conservative surgery. This conclusion is based on the results of various studies that have compared the outcomes of radical and conservative surgical interventions for liver hydatid disease. Radical surgery involves the complete removal of the cyst and surrounding tissue, which has been shown to significantly reduce the risk of postoperative recurrence. In contrast, conservative surgery, which involves partial resection or drainage of the cyst, has been associated with higher rates of complications and recurrence.

Although conservative surgery may be a good choice in some cases, such as when a cyst is located in a sensitive area or the patient is seriously ill, radical surgery is generally an effective way to prevent postoperative recurrence and provide timely treatment (16).

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percutaneous intervention (PAIR)
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Percutaneous intervention, also known as PAIR, is a minimally invasive procedure. This involves removing the cyst using a needle inserted into the skin. This is often combined with albendazole therapy to prevent cyst recurrence (16, 17).

Chemotherapy

Chemotherapy with albendazole or mebendazole is an alternative treatment option. These medications are effective in reducing the size of the cysts and can be used in combination with PAIR or as a standalone treatment. However, the efficacy of chemotherapy alone is limited, and it is often used in conjunction with other methods (*18*).

"Watch and Wait" Approach

In some cases, hydatid cysts are inactive and cause no symptoms. In these cases, a "watch and wait" approach may be recommended, with the cyst monitored for any

signs of activity or growth. This method is usually used for static cysts that do not cause any problems (19).

In general, treatment of cystic disease usually involves surgical removal of the cyst, which is the most effective method. However, if surgery is not possible or the cyst is located in a sensitive area, percutaneous drainage and chemotherapy using albendazole or mebendazole can be performed.

In humans, these drugs must be taken in high doses and for a long time, and they have undesirable side effects. Paying attention to these facts, it is very important to find new drugs with more effect and less side effects for the treatment of hydatid cyst. For this reason, it is important to identify and prepare effective drugs without side effects such as medicinal plants for the treatment of hydatid cyst.

Scolicidal effects of plant extracts

Over the past few decades, scientists have been searching for new safe and effective scolicidal agents to inactivate the contents of cysts. Recently, the study of the antiparasitic activity of medicinal plants is of great interest.

New studies have shown the high scolicidal activity of plants such as *Eucalyptus* microtheca (20), Myrtus communis (21), Sideritis perfoliata (22), Sambucus ebulus (23), Zingiber officinale (24). The hydroalcoholic extract of Pistachio Atlantica fruits has shown strong scolicidal activity under laboratory conditions (25). The phytochemical analysis of the plant extracts showed the presence of various bioactive compounds like flavonoids, alkaloids, tannins, and terpenoids. These phytochemicals appear to be responsible for the anti-protoscolices (anti-hydatid cyst) effects of the plant extracts.

The mechanisms by which these plant extracts kill the protoscolices are not fully understood, but may involve disruption of cell membranes, inhibition of enzymatic activities, and induction of oxidative stress. The concentration and exposure time of the plant extracts appear to be important factors in determining their scolicidal potency. In summary, the phytochemicals present in various medicinal plant extracts, such as alkaloids, flavonoids, and terpenoids, seem to be the key contents that confer the anti-hydatid cyst effects observed in these studies (26-29).

The identification of live and dead parasites using eosin dye

The identification of live and dead parasites using eosin dye is a technique employed in parasitology to distinguish between viable and non-viable parasites. This method is based on the principle that live parasites have intact cell membranes, which prevent certain dyes like eosin from entering the cell. Dead parasites, on the other hand, have compromised cell membranes, allowing the dye to penetrate and stain the cell (Fig3). In this method, a solution of eosin dye is mixed with the parasites, and the mixture is then observed under a microscope. Live parasites will not take up the dye and will appear as clear or transparent cells, while dead parasites will be stained red or pink due to the dye's ability to penetrate the damaged cell membrane. The reason for using eosin dye in this process is that it is a vital stain, which means it is excluded by live cells but taken up by dead cells. This property makes eosin dye particularly useful for distinguishing between live and dead parasites, as it allows for a quick and simple visual assessment of the parasites' viability (*30*).



Fig3. live and dead parasites using eosin dye. Live parasites (a). Dead parasites (b).

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Authors' Contribution

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SH.H., Z.S.

Writing original draft preparation, writing-reviewing and editing, SH.H

Ethics

Not Applicable.

Conflict of Interest

The authors declare that they have no conflicts of

interest to disclose.

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Data Availability

The data that support the findings of this study are available on request from the corresponding author.

References

- 1. M. Zeinali *et al.*, Human Cystic Echinococcosis in Different Geographical Zones of Iran: An Observational Study during 1995-2014. *Iranian journal of public health* **46**, 1623 (Dec, 2017).
- 2. M. Ebrahimipour, C. M. Budke, M. F. Harandi, Control of Cystic Echinococcosis in Iran: Where Do We Stand? *Trends in Parasitology* **36**, 578 (2020/07/01/, 2020).

- 3. M. Develoux, [Hydatidosis in Africa in 1996: epidemiological aspects]. *Medecine tropicale : revue du Corps de sante colonial* **56**, 177 (1996).
- 4. M. A. Cucher *et al.*, Cystic echinococcosis in South America: systematic review of species and genotypes of Echinococcus granulosus sensu lato in humans and natural domestic hosts. *Tropical Medicine & International Health* **21**, 166 (2016).
- 5. G. Grosso, S. Gruttadauria, A. Biondi, S. Marventano, A. Mistretta, Worldwide epidemiology of liver hydatidosis including the Mediterranean area. *World journal of gastroenterology* **18**, 1425 (Apr 7, 2012).
- 6. S. Adambekov, A. Kaiyrlykyzy, N. Igissinov, F. Linkov, Health challenges in Kazakhstan and Central Asia. *Journal of epidemiology and community health* **70**, 104 (Jan, 2016).
- 7. M. Moosazadeh *et al.*, Epidemiological and clinical aspects of patients with hydatid cyst in Iran. *Journal of parasitic diseases : official organ of the Indian Society for Parasitology* **41**, 356 (Jun, 2017).
- 8. C. E. Plummer, C. M. H. Colitz, V. Kuonen, in *Equine Infectious Diseases (Second Edition),* D. C. Sellon, M. T. Long, Eds. (W.B. Saunders, St. Louis, 2014), pp. 109-118.e3.
- 9. P. L. Moro, P. M. Schantz, in *Hunter's Tropical Medicine and Emerging Infectious Disease (Ninth Edition),* A. J. Magill, D. R. Hill, T. Solomon, E. T. Ryan, Eds. (W.B. Saunders, London, 2013), pp. 908-912.
- 10. D. Hanalioglu *et al.*, Anaphylactic shock following minor abdominal trauma as the initial presentation of Echinococcus cyst: a case report. *BMC Pediatrics* **22**, 89 (2022/02/12, 2022).
- 11. N. Khalili, P. Iranpour, N. Khalili, S. Haseli, Hydatid Disease: A Pictorial Review of Uncommon Locations. *Iranian journal of medical sciences* **48**, 118 (Mar, 2023).
- 12. J. M. Hart, F. Eshetu, S. Kassa, An unusual manifestation of hydatid disease: A case in a 20-year old male patient. *IDCases* **27**, e01359 (2022/01/01/, 2022).
- 13. L. J. Robertson, in *Encyclopedia of Food and Health,* B. Caballero, P. M. Finglas, F. Toldrá, Eds. (Academic Press, Oxford, 2016), pp. 219-224.
- 14. S. J. Condie, J. R. Crellin, F. L. Andersen, P. M. Schantz, Participation in a community program to prevent hydatid disease. *Public Health* **95**, 28 (1981/01/01/, 1981).
- 15. M. Reza, Seyed, Khoshnevis, Jalaluddin, P. Kharazm, Surgical treatment of hydatid cyst of the liver: Drainage versus Omentoplasty. *Annals of Hepatology* **4**, 272 (2005).
- 16. W. Farhat *et al.*, Radical versus conservative surgical treatment of liver hydatid cysts: A paired comparison analysis. *The American Journal of Surgery* **224**, 190 (2022/07/01/, 2022).
- 17. S. Nasseri-Moghaddam, A. Abrishami, A. Taefi, R. Malekzadeh, Percutaneous needle aspiration, injection, and re-aspiration with or without benzimidazole coverage for uncomplicated hepatic hydatid cysts. *The Cochrane database of systematic reviews* **2011**, CD003623 (Jan 19, 2011).
- 18. V. Velasco-Tirado *et al.*, Medical treatment of cystic echinococcosis: systematic review and meta-analysis. *BMC infectious diseases* **18**, 306 (Jul 5, 2018).
- 19. J. Hager, C. M. Sergi, Pediatric Echinococcosis of the Liver in Austria: Clinical and Therapeutical Considerations. *Diagnostics (Basel, Switzerland)* **13**, (Apr 4, 2023).
- 20. H. Mahmoodpour, A. Spotin, G. R. Hatam, A. Pourmahdi Ghaemmaghami, S. M. Sadjjadi, In vitro and ex vivo protoscolicidal effects of hydroalcoholic extracts of Eucalyptus microtheca on protoscoleces of Echinococcus granulosus sensu stricto: A light and scanning electron microscopy (SEM) study. *Experimental Parasitology* **251**, 108553 (2023/08/01/, 2023).
- 21. M. Benmarce *et al.*, Comparison of the Scolicidal Activity of Two Leaves Extracts of Myrtus communis from Algeria Against Echinococcus granulosus Sensu Lato Protoscoleces. *Acta Parasitologica* **69**, 839 (2024/03/01, 2024).

- 22. T. Çelik, M. Önderci, M. Pehlivan, Ö. Yumrutaş, F. Üçkardeş, In vitro scolicidal effects of Sideritis perfoliata extract against Echinococcus granulosus. *International Journal of Clinical Practice* **75**, e14498 (2021).
- 23. S. Gholami, B. Rahimi-Esboei, M. Ebrahimzadeh, M. Pourhajibagher, In vitro effect of Sambucus ebulus on scolices of Hydatid cysts. *Eur Rev Med Pharmacol Sci* **17**, 1760 (2013).
- 24. M. Moazeni, A. Nazer, In vitro lethal effect of Zingiber officinale R. on protoscolices of hydatid cyst from sheep liver. *Microbiology Research* **2**, e25 (2011).
- 25. M. Ghalavand, H. Esmaeili-Gouvarchin-Ghaleh, M. Mirzaei-Nodooshan, S. Vazifedost, S. Mohammadi-Yeganeh, An evaluation of the effects of Pistacia atlantica gum hydro-alcoholic extract on the phagocytosis ability of macrophages and atherosclerosis development in hypercholesteremic rats. *ARYA atherosclerosis* **18**, 1 (Jul, 2022).
- 26. S. H. Shahraki, F. M. Javar, M. Rahimi, Quantitative and Qualitative Phytochemical Analysis of <i>Manilkara zapota</i> (Sapodilla) Extract and Its Antibacterial Activity on Some Gram-Positive and Gram-Negative Bacteria. *Scientifica* **2023**, 5967638 (2023/12/26, 2023).
- 27. H. Sadeghi *et al.*, Iron oxyhydroxide nanoparticles: green synthesis and their cytotoxicity activity against A549 human lung adenocarcinoma cells. *Rendiconti Lincei. Scienze Fisiche e Naturali* **33**, 461 (2022/06/01, 2022).
- 28. S. H. Shahraki, T. Ahmadi, B. Jamali, M. Rahimi, The biochemical and growth-associated traits of basil (Ocimum basilicum L.) affected by silver nanoparticles and silver. *BMC Plant Biology* **24**, 92 (2024/02/06, 2024).
- 29. M. Babaei, L. Shabani, S. Hashemi-Shahraki, Improving the effects of salt stress by β-carotene and gallic acid using increasing antioxidant activity and regulating ion uptake in Lepidium sativum L. *Botanical Studies* **63**, 22 (2022/07/16, 2022).
- 30. L. Wen *et al.*, In vitro and in vivo Effects of Artesunate on Echinococcus granulosus Protoscoleces and Metacestodes. *Drug design, development and therapy* **14**, 4685 (2020).