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OSTEO-HYDATIDOSIS: EPIDEMIOLOGY, CLINICAL MANIFESTATIONS, AND ADVANCEMENTS IN DIAGNOSIS AND TREATMENT OF *ECHINOCOCCOSIS*

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Abstract

Osteo-Hydatidosis, a zoonotic disease caused by the larval stage of the *Echinococcus granulosus* tapeworm, presents a significant global public health concern due to its potential morbidity and mortality. The slow growth of the parasite in the spine leads to symptoms primarily caused by spinal cord compression. It is more common in endemic areas and can cause significant mortality and morbidity. It is difficult to diagnose and treat osteohydatidosis effectively because no specific diagnostic methods are available. In most cases, surgical intervention is required to remove the cyst, decompress the spinal cord, and stabilize the affected area. This study aimed to provide insights into the clinical characteristics, diagnostic methods, laboratory findings, treatment options, and patient outcomes associated with this condition. Additionally, the study emphasized the challenges in diagnosing and treating osteohydatid disease because of the lack of specific diagnostic tools. A diagnosis of osteohydatid disease is possible in areas where it is endemic, and early diagnosis and treatment are crucial. This review summarises the current state of osteo-hydatidosis diagnosis and treatment. The healthcare sector is better positioned to face the complexity of this disease as a result of its embrace of cutting-edge technologies and multidisciplinary approaches, which will ultimately lead to improved patient treatment and pave the way for a more complete control and management strategy.

Keywords: Osteo-hydatidosis**,** *Echinococcus Granulosus*, Vertebral, Surgery, Chemotherapy.

INTRODUCTION

Osteo-Hydatidosis, caused by the larval stage of the parasitic tapeworm *Echinococcus granulosus*, remains a formidable health challenge worldwide. This zoonotic infection affects various organ systems, with the potential for severe morbidity and mortality. The complexity of Osteo-Hydatidosis lies not only in its intricate lifecycle but also in the challenges posed by accurate diagnosis and effective treatment. The parasite *Echinococcus*, which is transmitted from animals to humans, causes several types of *echinococcosis* [1]. Hydatid *echinococcosis* is caused by the parasite *E. granulosus* [2]. *Echinococcosis*, a zoonotic parasitic disease, is caused by the larval form of the *Echinococcus* tapeworm species [3]. It manifests in clinically significant forms such as *cystic echinococcosis* (CE), caused by the larval stage of *E. granulosus*, and *alveolar*

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echinococcosis (AE), and the latter is often called "worm cancer" due to its high mortality rate [4]. The World Health Organization (WHO) reports an annual infection rate of more than 50 per 100,000 people in *echinococcosis*-endemic locations. There are several cases in some regions of Central Asia, East Africa, and Argentina [3]. *Echinococcosis* is primarily transmitted through the fecal-oral route, which involves direct contact with infected definitive animal hosts like dogs or ingestion of parasite eggs present in contaminated water, soil or food [5]. Hydatid disease persists despite its prevalence in various regions where livestock farming is practiced worldwide. Due to the lack of symptoms in the early stages, hydatid disease of the bone is often diagnosed only when severe radiologic lesions have developed. The most common sites of these bone lesions are the spine and pelvis, where they can cause unbearable pain. When it comes to treating bone hydatidosis, chemotherapy is ineffective. Similarly to oncological treatments, a wide surgical resection is typically necessary [6,7]. The life cycle of *Echinococcus* spp. is outlined in this review, and *echinococcosis* epidemiology, transmission, and clinical manifestations are also discussed. We highlighted current developments in the diagnosis, treatment, and control of CE and how they function in mammalian hosts; this knowledge is crucial for creating new medicines and therapies to combat *echinococcosis*.

Disease transmission and Life cycle

E. granulosus primarily inhabits the small intestine in its adult form within the definitive host. The tapeworm comprises three main parts the head (scolex), the neck, and the tail [8]. The parasite attaches itself to the intestinal wall of the host using two or more suckers on its head and, under certain conditions, a rostellum or a knob with tiny hooks. The tapeworm strobila is connected to its scolex through a short neck, which consists of a chain of interconnected segments known as proglottids. These proglottids form a ribbon-like chain and contain both male and female reproductive organs, enabling them to produce eggs for the parasite. The proglottids are initially formed in the neck region of the tapeworm and then descend along the strobila while new segments are continually added above them [9]. Once the proglottids of the tapeworm become gravid (containing eggs), the tapeworm releases them. Gravid proglottids can produce instantly contagious eggs discharged in feces [10]. When contaminated waste is released into the environment, it has the potential to infect an intermediate host. When the eggs hatch in the intermediate host small intestine, oncospheres are released. These oncospheres have six hooks that enable them to penetrate the mucosa of the intestinal wall. From there, they enter the bloodstream and can travel to various organs, with the liver and lungs being the most common destinations [11].

Hydatid cysts typically contain clear fluid and have a spherical shape. The presence of parasites initiates a granulomatous inflammatory response, forming fibrous tissue that surrounds and isolates the cysts. To become infected, the definitive host must consume the intermediate host organs that contain the hydatid cysts. Once ingested, the protoscolices within the cysts are released. These protocolises attach to the intestinal

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mucosa, undergo further development, and mature into tapeworms within the intestinal lumen of the definitive host [12]. *Echinococcus granulosus* cestodes can unintentionally use humans as intermediate hosts. There are various strains of *Echinococcus granulosus*, each characterized by its distinct combination of phenotype and genotype. Regardless of these variations, it has been observed that all parasite strains uses dogs and other canids as definitive hosts. In the life cycle of *E. granulosus*, animals such as horses, cattle, sheep, pigs, camels, and goats act as intermediate hosts. On the other hand, foxes, wolves, and dogs serve as definitive hosts. Dogs are crucial definitive hosts, while other animals function as intermediate hosts. Herding dogs can become infected by scavenging on the remains of cattle left in pastures or by consuming contaminated offal from home slaughter. *Echinococcosis* is transmitted from infected dogs to humans when the faeces of the dogs contaminate the environment, and humans unintentionally ingest the contaminated material. The parasite eggs can remain viable for extended periods and withstand dehydration, enabling transmission to humans even without direct contact with intermediate or vector animals. Once humans ingest the eggs, they hatch in the digestive system, releasing oncospheres. These oncospheres then penetrate the intestinal mucosa and enter the bloodstream. They reach various visceral organs through the bloodstream, forming larval cysts and developing into adult parasite stages [13].

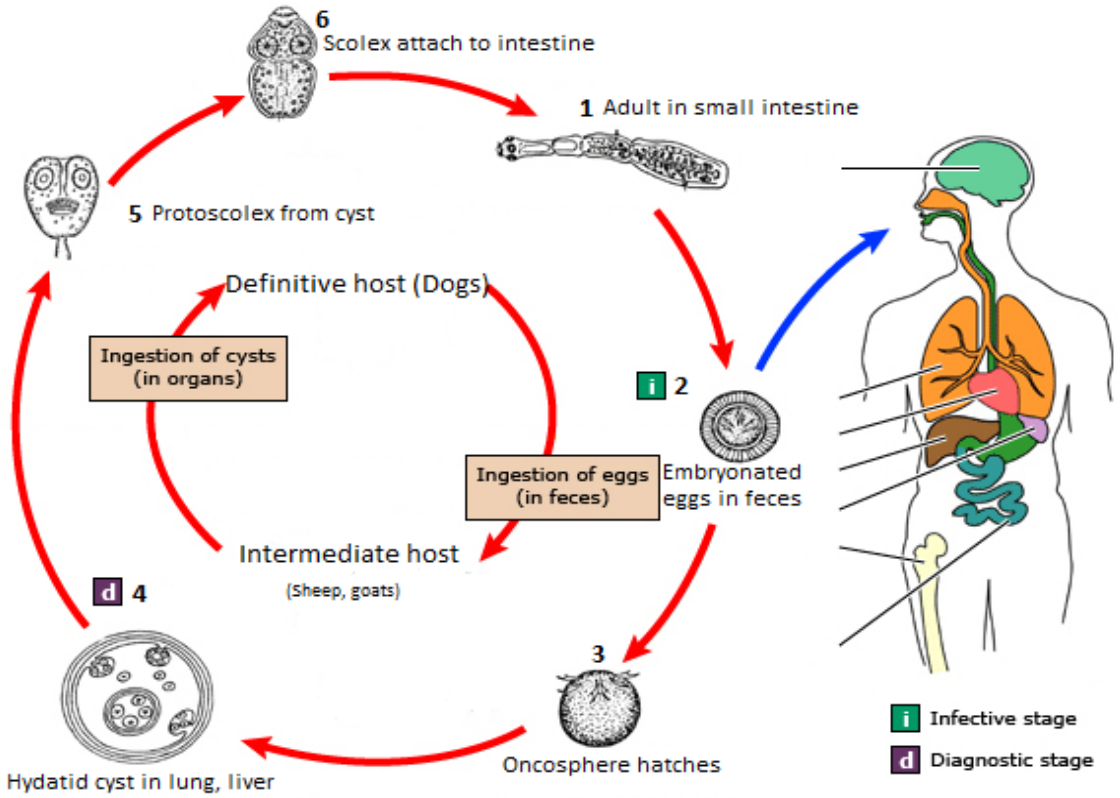

Figure 1: Life cycle

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Structure of the Hydatid Cyst

The hydatid cyst is composed of three layers, The outer layer is pericyst, composed of modified host cells, forms a fibrous and dense protective zone that serves as a barrier; the middle-laminar membrane, which lacks cells, acts as a barrier allowing the nutrients passage; and, the inner germinal layer is responsible for producing the scolices and the laminated membrane [14]. Daughter vesicles (brood capsules) are small spheres containing the protoscolices formed from the germinal layers. The germinal layers and the middle-laminated membrane together constitute the actual wall of the cyst, commonly referred to as the endocyst. It is worth noting that the acellular laminated membrane is occasionally called the ectocyst. These daughter vesicles adhere to the mother cyst germinal layer through a pedicle before developing into daughter cysts. The cysts look like grapes when viewed at a distance. In cases of bone disease caused by *E. granulosus*, daughter cysts can sometimes rupture through the wall of the mother cyst. This can result in the spread of the infection and the formation of other cysts in the surrounding bone tissue [15]. Sodium chloride, lipids, glucose, proteins, ions, and polysaccharides are all components of cyst fluid, which is otherwise colorless or pale yellow in appearance and has a neutral pH. Antigens and maybe scolices and hooklets can be found in the fluid. When vesicles rupture inside the cyst, scolices are released into the cyst fluid, forming a white sediment called hydatid sand [16].

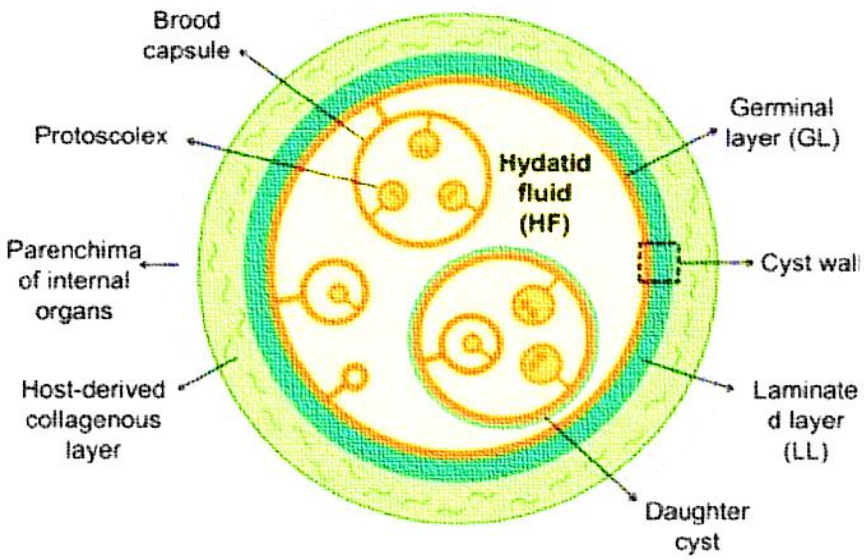

Figure 2: Structure of the Hydatid Cyst

Topographic Aspects of Vertebral, Pelvic, and Long Bone *Echinococcosis*

Vertebral *Ecchinococcosis*

Vertebral *echinococcosis* is the most common hydatid disease, with an incidence of 42% and 46%. The involvement of CNS in *echinococcosis*, particularly when it affects the brain

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or spinal cord, poses the most severe neurologic danger and presents significant challenges in surgical eradication Vertebral echinococcosis is an unusual form of cystic echinococcosis, a parasitic disease brought on by the larval stage of the *Echinococcus granulosus* tapeworm. The vertebral column is invaded by parasitic cysts in this form of echinococcosis, providing particular challenges in diagnosis and treatment. Its propensity to cause spine abnormalities, neurological deficits, and substantial morbidity, despite its rarity, underscores the significance of thorough investigation and comprehension [16,17]. Due to its similarity to Pott disease and spondylitis, a correct diagnosis might be challenging. Hydatid disease typically isn't discovered until after it has caused severe damage to the nervous system and bone. In costovertebral shapes, the vertebrae come first in the locoregional evolution, followed by the ribs. Although the spinal column retains flexibility, a paravertebral abscess is common, often developing slowly and aphetically in the back. According to Karray et al. [18], *Echinococcus granulosus*' complex life cycle is deeply rooted in the aetiology of vertebral echinococcosis. Tapeworms lay eggs in the intestines of definitive hosts, which are typically canids, and then shed those eggs into the surrounding environment. The eggs release oncospheres that pierce the intestinal wall and travel throughout the body via the bloodstream when they are consumed by intermediate hosts, frequently herbivores or humans. These oncospheres cause vertebral echinococcosis by forming hydatid cysts inside the vertebral bodies, which can cause a number of symptoms [19].

Pelvic *Echinococcosis*

According to Chen and Zhao [19], 16% of osseous hydatidosis is caused by *pelvic echinococcosis*, but Iken et al. [20] put that number far higher at 28%. In terms of prevalence, it is the second most common subtype of this disease. Hydatid lesions thrive in the pelvis due to soft, avascular tissue prevalence. The clinical latency of the disease allows for the possibility of parasite invasion in the coxofemoral and sacroiliac joints even after the disease has spread to the pelvis, resulting in a significant change in the prognosis. This can happen via invasion of the sacroiliac ligaments or through the hip articulations. Abscesses tend to spread within both the endopelvic and extrapelvic cavities. The extrapelvic abscess can travel through the more prominent sciatic notch from the buttock and extend up the thigh. As a result, the initial clinical sign may be pain in the pelvis or buttocks, which can occur due to compression of the sciatic, femoral, and femorocutaneous nerves. Tumors and pregnancy problems can be warning signs for various diseases. The prognosis is conditional on whether the sacroiliac or coxofemoral joints are involved. Surgical removal becomes risky when this happens, and severe mutilations are inevitable.

Long Bones *Ecchinococcosis*

Fifteen percent to thirty percent of osseous hydatidosis is caused by *echinococcosis* of the long bones. Femurs and tibias are the most common bones to be damaged [21]. The "Panosteoechinoccocosis of Costantini" [30] occurs when the parasite first establishes itself in the metaphysis and spreads to the diaphysis and both epiphyses. The

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surrounding bone and soft tissues are also obstructed. Tumors and pathologic fractures are the most common indicators of disease. Osseous *echinococcosis* fractures can be set without surgical intervention. The prognosis for these areas remains poor due to the late discovery of the disease, typically when the lesions are already severe. Extreme measures such as limb amputation or joint disarticulation are highly mutilating and do not guarantee that the problem will not recur. Infection and recurrence are common complications of prostheses [22].

Table 1: Topographic Aspects of Vertebral, Pelvic, and Long Bone *Echinococcosis*

Aspect	Description	Ref.
Vertebral *Echinococcosis*	• The most common form of osseous hydatid disease • It involves the vertebral column, especially the dorsal spine • Formation of paravertebral abscesses • Potential for paralysis due to spinal cord compression • Often misdiagnosed as Pott disease or spondylitis initially • Challenging Diagnosis and Treatment • Surgical eradication is required to prevent neurologic complications	[21, 23-25]
Pelvic *Echinococcosis*	• The subtype of osseous hydatid disease • It affects the pelvic region • Involves sacroiliac and coxofemoral joints • Thrives in soft, avascular pelvic tissues • Formation of abscesses • Abscesses can spread within and beyond the pelvic region • Causes pain and nerve compression • Risky surgical removal if joints are involved • Potential for severe mutilations	[3,25,26]
Long Bones *Echinococcosis*	• Involvement of femurs and tibias • Parasite establishes in the metaphysis and spreads to diaphysis and epiphyses • "*Panosteoechinoccocosis of Costantini*" condition • Obstruction of surrounding bone and soft tissues • Pathologic fractures and tumors • Late discovery and severe lesions • Poor prognosis • Limb amputation or joint disarticulation may be necessary • Infection and recurrence risks with prostheses	[17,26]

Epidemiology

Due to the transmission of *Echinococcus granulosus* by domestic dogs in regions where livestock is raised, the disease can be found in any part of the world [27]. However, the *echinococcosis* incidence varies from region to region depending on whether a country has nomadic or seminomadic goat flocks and sheep, which serve as intermediate hosts [28]. Countries in the temperate zone, including southern and central Russia, the Mediterranean, South America, Central Asia, Australia, China, and north and east Africa, have a higher reported incidence. The Mediterranean area is now believed to have an

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endemic *echinococcosis* population. Both sexes appear equally at risk for contracting *echinococcosis* [29]. *Echinococcosis* does not show a specific age preference, as it can infect individuals of all age groups. However, studies have reported a relatively higher prevalence of the disease in patients aged 30-36 years [29]. The liver's right lobe is more prone (about 70%) to hydatid cyst development than any other part of the liver. The lungs are the second most prevalent site of involvement (20-30%). Other less commonly involved organs are the heart, brain, and bones. The incidence of *osseous echinococcosis* is low (0.5–4%) [30]. Spinal involvement is the most frequent form of *osseous echinococcosis*, although considered rare overall, occurring in approximately 0.2% to 1% of cases [31]. Among the spinal locations affected by *osseous echinococcosis*, the thoracic spine is the most common, accounting for approximately 50% of cases. The lumbosacral region is the next most frequently involved (about 29%), followed by the lumbar spine (about 21%). Many patients with thoracic spine *echinococcosis* have a prior history of extraspinal *cystic echinococcosis*, most commonly affecting the liver, lungs, kidneys, and soft tissues. Some individuals may have a history of surgically treated lung *echinococcosis*, which could explain the higher occurrence of thoracic spine involvement [32]. In thoracic spine *echinococcosis* cases, the hydatid cysts typically extend beyond the vertebral bodies and can affect the spinal cord, intervertebral discs, and posterior spinal elements. In some instances, the cysts may also grow within the spinal canal [31,32].

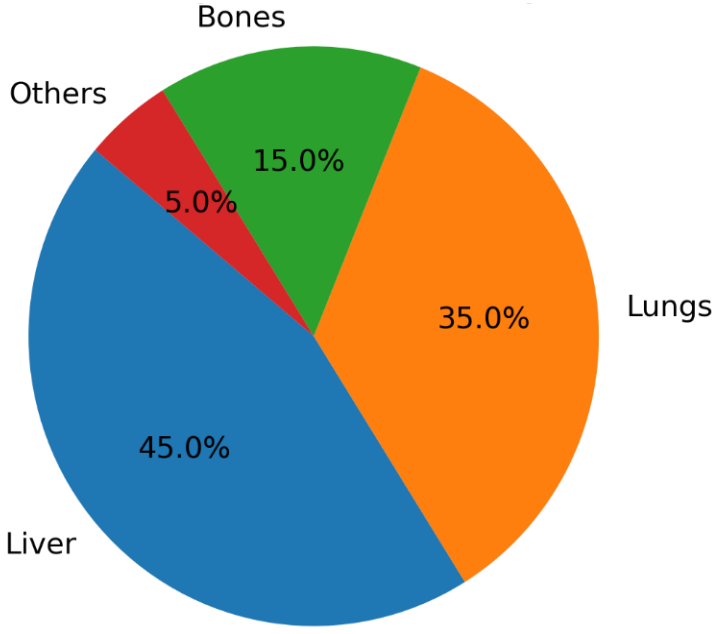

Figure 3: Distribution of Osteo-Hydatidosis caused by affected organs

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Classification

WHO classification

The WHO Informal Working Group on *Echinococcosis* (WHO-IWGE) characterized hydatid sores into three clinical groups as follows: (1) The "transitional" category, which includes cysts with a detached endocyst membrane (CE3a) and cysts that are primarily solid but include daughter vesicles (CE3b [32] (2) The "active" group of developing cysts in *echinococcosis* can be classified as unilocular (CE1) or multivesicular with daughter vesicles (CE2). These cysts are typically fertile and contain viable protoscoleces, which are the larval forms of the parasite (3) Solid contents with calcification (CE5) and solid contents (CE4), both of which are often nonviable, make up the "inactive" category. The World Health Organization categorization provides a complete foundation to build decisions about treatment and monitoring [33].

Classification Based on Diagnostic Imaging Appearance

Hydatid cysts are subdivided into four categories according to their appearance on diagnostic imaging [34-36].

Simple Cyst

This is the first and most aggressive stage of hydatid disease [34]. When first diagnosed, a hydatid cyst would have the appearance of a unilocular cystic lesion with little internal architecture, a well-circumscribed, with or without internal hydatid sand or septations, and with a frequent elevation of the septa and cyst wall on post-contrast CT [35]. Differentiating type I hydatid cysts from simple liver cysts can be achieved using the Diffusion-Weighted Imaging (DWI) sequence [36].

Cyst with matrix and daughter cysts

Cysts, which contain daughter cysts and a matrix, are the most prevalent and infectious form of the hydatid parasite [34]. Multiple septa, which indicate the partitions between the daughter cysts inside the mother cyst, are often distributed peripherally in cysts. This type can have various appearances depending on the maturity and arrangement of the daughter cysts: (1) A characteristic feature of hydatid cysts is the presence of multiple daughter cysts arranged around the central mother cyst. These daughter cysts are often seen in a "wheel spoke appearance," where they radiate outward from the center, creating a distinctive pattern;" (2) multiple irregular daughter cysts can occupy the central cyst, making a distinct "rosette appearance." The daughter cysts are irregularly shaped and occupy the space within the primary cyst, resembling the petals of a rosette;" and (3) the third subtype of hydatid cysts can exhibit a hyperdense matrix, meaning it appears denser on imaging studies compared to other cyst types. When seen on MRI, offspring cysts have a weak signal or are isointense to the matrix [35,36].

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Calcified cysts

Hydatid disease is typically asymptomatic, impracticable to detect, and presents minimal risk of dissemination during its third stage, characterized by calcified cysts [34]. It shows up as a low signal intensity region on an MRI, a circular hyperdense lesion on CT, and a lesion with calcification demonstrates posterior acoustic shadowing on ultrasound. CT best diagnoses calcified hydatid cysts, the gold standard imaging modality [35].

Complicated hydatid cyst

This includes hydatid cysts of Types I and II ruptured or developed a superinfection. Diagnosing complex hydatid cysts mostly depends on CT and MRI scans [35,36]. Age-related degradation of the parasite membrane or a defensive mechanism account for 50% of hydatid cyst ruptures [37,38]. When a hydatid cyst grows to a significant size, it can compress the adjacent bile duct or even perforate into it, both of which can lead to biliary duct dilatation. Internal ruptures allow the cyst contents to enter the biliary ducts, whereas external ruptures allow the contents to pour into the peritoneal cavity and spread the infection. When a hydatid cyst ruptures, germs can readily enter the cyst and cause hydatid disease [39]. Contrast-enhanced CT and MRI scans can reveal the presence of air within a cyst because it makes the cyst walls seem thicker and more distinct [40]. Exophytic growth of hydatid cysts can occur on the naked surface of the liver, allowing migration through the diaphragm to reach the lung or mediastinum. Alternatively, the cysts can also migrate through the gastrohepatic ligament into the peritoneal cavity [41]. In most cases, hepatic hydatid disease is the underlying cause of peritoneal seeding. It can happen after an operation to remove hepatic hydatid cysts. Imaging techniques such as CT and MRI are helpful in the diagnosis of peritoneal hydatid cysts [34].

Table 2: Classification

Classification		Description	Ref
WHO classification	Active	Developing cysts, fertile with viable protoscoleces.	[32,33]
	Transitional	Cysts with detached endocyst (CE3a) or solid cysts with daughter vesicles (CE3b).	[32-35]
	Inactive	Solid contents with calcification (CE5) or Solid contents (CE4).	[34,35]
Based on Diagnostic Imaging Appearance	Simple Cyst with no Architecture	Early and aggressive stage of hydatid disease with well-defined unilocular cysts.	[36-37]
	Cyst with daughter cysts and matrix	The most common and infectious hydatid cysts contain daughter cysts and a matrix.	[35-36]
	Calcified cysts	The asymptomatic stage is characterized by calcification and minimal risk of dissemination.	[36-40]
	Complicated hydatid cyst	Ruptured or superinfected cysts with potential complications are diagnosed through CT and MRI scans.	[34-39]

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Symptoms and Clinical Features

The brain, spleen, kidney, and heart are all at risk, in addition to the liver (70%) and lungs (20%), which are the most commonly affected organs. The liver is where most AE lesions start [42]. Most AE and CE patients seek medical attention late in the disease phase. According to population screening, more than half of CE liver cysts in humans do not change in size in 10 years, and one-third develop less than 3 cm; cyst growth in cases with a longer follow-up was 0.7 cm [43]. Early CE and AE are generally asymptomatic, delaying diagnosis. AE lesions and CE cysts can be asymptomatic for 10-15 years. As a result, echinococcosis affects a tiny percentage of youngsters [44]. Clinical symptoms of liver cysts often manifest themselves when the bile ducts, portal vein, hepatic veins, or hepatic artery are physically squeezed or injured by a liver cyst larger than 10 centimetres in diameter or when the cyst or organ occupies more than 70% of the organ volume [45]. Compression or injury to the lungs or other brain regions may cause a variety of symptoms, some of which may be fatal. Due to compression of surrounding essential tissues, even relatively sized cysts in any organ may cause symptoms. Patients with symptomatic CE and liver cysts report upper abdomen pain and loss of appetite; jaundice cysts may result from bile duct constriction. Cyst rupture into the bronchi can cause the discharge of hydatid materials and coughing or hemoptysis, as well as chest pain. Brain cysts may cause neurological symptoms such intracranial hypertension, epilepsy, and paralysis. [46]. Fever, eosinophilia, urticaria, and anaphylactic shock can result from cyst rupture in any organ [47,48]. Due to the risk of catastrophic allergic reactions from cyst rupture or even slight fissures, CE cyst penetration has long been prohibited because.

The name 'granulosus' refers to a characteristic of echinococcosis (AE and CE), which has a high IL-5 level, a key component of the Th2-type immune response [49]. Eosinophilia and allergic reactions are uncommon in alveolar echinococcosis (AE), despite the fact that IgE antibodies have been found and basophil activation has been shown in some cases [50]. This is because parasite lesions have thick fibrosis that limits vesicle fluid leakage. However, infrequent blood diffusion of lesion pieces may cause these effects [49]. AIDS patients with CE have faster cyst formation, suggesting immune suppression may contribute to CE. A recent theory suggests that CE may increase community cancer growth due to immune surveillance failures caused by Echinococcus-induced tolerance. A hospital medical information system evaluation found no difference in cancer occurrence between cystic echinococcosis (CE) and non-CE patients. This shows that these two frequent diseases may coexist, especially in CE-endemic areas [99]. However, the malignancy or its treatment appears to have less impact on CE development or progression than AE [51].

Diagnosis of Hydatid Disease

Due to massively different sensitivities and specificities, serological antibody-detecting tests employing distinct native antigens are only employed for confirming the diagnosis [51]. Up to 80% and 93% sensitivity and specificity have been achieved in diagnosing hydatid disease utilizing ELISA employing the synthetic peptide p176 [50]. Medical

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imaging modalities, such as abdominal ultrasound imaging, a chest X-ray, and a CT of the belly, brain and chest, are used to identify hydatid disease [51].

Serological assay

Human immunoreactivity toward hydatid cysts is proportional to the infecting organism's growth rate, health, and geographic location. Immunoreaction is greater in damaged than in healthy hydatid cysts. A severe allergic reaction, or even death, can occur if the skin is ruptured. When the hydatid cyst is old, hardened, or dead, serological testing often results negative [52]. Due to the absence of a fibrous capsule and the cyst contiguity with human tissue, Lightowlers et al. [53] observed a strong immunoreaction in cases with bone hydatid cyst disease. Now, two serologic tests are used to diagnose hydatid cyst disease. The primary antigenic components of hydatid fluid and protoscoleces are Ag 5 and Ag B25, detecting the antibodies in the blood serum of patients [54]. The diagnosis uses specific antibody tests, such as the counter immune electrophoresis, Casoni test, indirect haemagglutination, gold-labeled antibody, and enzyme-linked immunosorbent assay. Serologic assays for spinal *echinococcosis* are only 25% sensitive and 56% specific and infected children may present with normal serology [55]. The Casoni test, counter-immune electrophoresis, and indirect haemagglutination are commonly referred to as the "three components of hydatid cyst examination." However, it is important to note that using native antigens directly derived from hydatid cyst fluid without undergoing purification can result in a relatively high occurrence of false positive outcomes and limited sensitivity. Due to its high specificity and sensitivity, ELISA is typically employed as a confirming test [56]. The final diagnosis rate of identifying IgG1 by ELISA is 97.7%. The detection of IgM, IgG, and IgA combinations in patient plasma has a 98.0% specificity [57].

ELISA and the gold-labeled technique are two of the 'eight tests of immune diagnosis,' which together identify four different forms of antigen: cephalomere antigen, cyst fluid antigen, half-purified cyst fluid antigen, and alveolar *echinococcosis* antigen. The detection of IgG-specific subclass antibodies, specifically IgG4 and IgG1 isotypes, in cases of cystic *echinococcosis* (CE) and alveolar *echinococcosis* (AE) holds potential significance. This approach may offer the possibility of early disease detection and identification of chronic infections [58,59,60]. An eight-test battery is the most sensitive and specific serological approach, achieving up to 91.9% specificity and 92.6% sensitivity. The detection of CE-specific total IgG antibodies was used to evaluate disease activity after therapy in 28 individuals with CE [58]. This may also give a stronger association with hydatid patient prognosis following medical treatment [61]. Using an ELISA using crude horse hydatid cyst fluid as antigen, we found that the concentrations of CE-specific total IgG2, IgG1, and IgG antibodies were considerably higher at diagnosis compared with IgG4 and IgG3 antibodies [60,61]. For hydatid cerebrospinal disease, a diagnosis may present some challenges by serological test; nonetheless, the IgG2 antibody response offered the best indicator of disease activity throughout post-treatment follow-up. The primary hydatid antigen is 60 KD; therefore, a serological mistake may arise since the

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blood-brain barrier only allows molecules with a mass of roughly 40 KD to pass freely [62].

Laboratory tests

Eosinophilia, a high level of eosinophils in the blood, is frequently observed in various parasitic infections [63], and common laboratory markers used in infections, such as estimated sedimentation rate (ESR), WBC count, and C-reactive protein (CRP), are often within normal range and they are variable findings [64]. Whole parasites or parasite organelles and soluble antigens produced from cyst fluid are employed as antigen. In Western Blot analysis, the antigens are denatured and separated by electrophoresis. Subsequently, they are transferred onto a nitrocellulose membrane for further analysis. The test is considered positive if an enzymatically colored response occurs following the patient's serum incubation and, subsequently, with an anti-human IgG conjugate. The Western Blot method enables the analysis of molecular weights of the detected antigens. The hydatid disease can be detected with the help of a hypersensitivity-based skin test called the Casoni intradermal skin test. In a diagnostic method previously used for hydatid disease, a sterile fluid from a hydatid cyst is injected into one arm. In contrast, normal saline is injected into the other arm as a control. If a wheel response is observed at the injection site within 30 minutes, it is a positive indication of a hypersensitivity reaction, specifically of type I. However, caution must be exercised to prevent an anaphylactoid reaction. Once a significant diagnostic tool, serologic assays have primarily replaced this test, which offers greater sensitivity, specificity, and safety. *Echinococcosis* is diagnosed less reliably using laboratory testing, although they can help identify an echinococcal infection or help confirm the diagnosis if cysts are seen on imaging [64].

Imaging

Multiple, expansile cavitary regions without sclerosis or periosteal response, moth-eaten osteolytic, and posterior spinal elements are substantially involved. Multiple osteolytic lesions with trabeculae, calcification of adjacent soft tissues, and cortical thinning from echinococcal cysts are all seen on radiographs. Multilocular osteolysis on radiographs with a hazy bone picture, condensation, and no osteophytes or periosteal response suggest echinococcosis [65]. Because no specific features are consistent with echinococcosis, radiographs often misdiagnose lesions. Ultrasound can detect liver echinococcosis. This treatment's safety, non-invasiveness, and low cost make it valuable in low-income and developing nations where echinococcosis is common [66]. Due to the hazards and superiority of MRI in visualising spinal cord disorders, myelography is performed less often [67]. While radiographs show the same things, CT scans are more comprehensive and can detect tiny cysts. Echinococcosis may show erosion and multiple cysts on vertebral bodies and arches. The radiological finding "double layer arcuate calcification" strongly suggests echinococcosis above other cystic illnesses. MRI is better than CT for assessing surgical reappearances. MRI can be shown in any plane and provides better contrast between soft tissues than CT [68]. Hydatid cysts appear as fluid-filled lesions with septation, thin walls, and uneven branching on MRI. This resembles a

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grape cluster at various levels. Paravertebral muscles have multiple big spherical cystic lesions, some with smaller cysts [69].

Biopsy

In certain cases, CT or ultrasound-guided fine needle aspiration is employed to evaluate abdominal disease related to *echinococcosis*. In spinal hydatid disease, because of the high rate of bone association, cyst burst is more typical, prompting hypersensitivity and further disease seeding [70]. In situations where surgery is not feasible, there have been documented cases where cysts have been drained for therapeutic purposes in individuals.

Differential Diagnosis

Pott's disease can sometimes resemble hydatid disease due to its involvement of the spine and its occurrence in similar geographic regions as hydatidosis. Pott's disease is characterized by various symptoms, including a decline in the patient's general health, localized difficulty in specific spinal segments, fistulation of abscesses, early discomfort in the intervertebral disks, and a tuberculous background. In contrast, parasites in other spondylitis syndromes, such as diskitis, are less likely when radiographic signs of reconstruction, osteosclerosis, and serodiagnosis are observed. Conditions such as spinal metastases, aneurysmal cysts, Kahler's disease, chordoma, and vertebral plasmacytoma should also be considered differential diagnoses in such cases [71]. The liver is the most frequent organ hydatid cysts affect (75% prevalence) [72], followed by the lung (15%) [73], and the spleen, kidneys, and brain (5% prevalence) [74]. Depending on their location and severity, hydatid cysts can present a wide range of imaging characteristics [75]. However, they can manifest similarly to lesions of many bones and typically cause a diagnostic challenge before surgery involving bones and muscles. Because of their similarity to tumors, such as skeletal TB and musculoskeletal fungal infections, MRI is the recommended imaging technique for musculoskeletal hydatid cysts. The imaging results, patient's history, and *Echinococcus* antibodies contribute to a possible diagnosis. Minimizing bone damage and consequences requires a quick diagnosis [76]. It is possible that hydatid cysts won't be diagnosed until after surgery and a subsequent biopsy.

Hydatid Disease of Vertebral

Hydatid disease of the spine has a vertebral body lesion. One or more central or lateral holes without obvious boundaries, flowing together, oval or rounded, divided by a "bunch of grapes" wall, can be seen as the initial posterior arch lesion; Two other odd roentgenographic phenomena that can occasionally be seen are osteolysis without evident boundaries or a macrobiotic view with polycyclic contours. Later, the lesion extended to the parabrachial region, canal, and other bones, including the ribs and surrounding vertebrae. After this, the diagnosis is usually made. Multiple levels of spinal compression result from vertebral infection. Cuneiforms call this compression a flat cake or lateral asymmetry. Lateral spine injury ends with the spinal disc [78]. Osteous

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hydatidosis abscesses imply soft tissue disease. X-rays show spherical or polycyclic, calcified, swelling or hemiswelling paravertebral opacity. Mediastinal opacity in the rear or dorsal region results. The signs of spinal hydatidosis are also seen in spondylitis and, more typically, Pott's disease [79]. The ribs or vertebrae might lead to neighbouring bones. A "coastal affection." is a neck, head, or posterior arch lesion. The dorsal spine and ribs always have hydatidosis [80]. When the initial lesion spreads, upper and lower vertebrae show similar symptoms. Despite substantial lesions, keeping vertebra global structure and disc thickness is crucial to diagnosis [81]. Hydatidosis and spondylitis are difficult to distinguish in later stages due to disc compression and vertebral degeneration. Widening of the canal or foramen, increased interpedicular distance, and scalloping of the posterior or internal pedicle wall are signs of spinal canal expansion [81].

Hydatid Disease of the Pelvis

Typically, the ileum is the first pelvic structure affected; however, the ischium or the superior pubis ramus may be affected first. The radiographic results reveal many lacunae of varying widths that join to produce a sizable osteolysis region with a waffle shape. An unusual hollow or worm-eaten appearance can occasionally be spotted. Hips/sacroiliac joints and adjacent vertebrae are the primary sites of involvement [82].

Hydatid Disease of Long Bones

Metaphyseal and epiphyseal sites are common for the first lesion in long bones, with further damage occurring in the diaphysis and surrounding bones [69]. Cysts can be either monolocular, bilocular, or multilocular on radiographs. In the first, irregular oval or polycyclic nonspecific lacunae of varying sizes are found. The most seen is a polycystic or invading appearance with several loci. In either the epiphysis or the metaphysis, you can see a cluster of rounded or oval lacunae varying in size. When the lesions develop to this latter stage, the diaphysis becomes enlarged. All lesions lack distinct borders. Long-term maintenance of the bone's overall appearance and articular space is possible. Without a periosteal response, the inner cortical region thins and erodes. The infection causes irregular lacunae with thickened backlines, increased cortical thickness, and occasionally a periosteal reaction [81].

Rare Sites of Hydatid Cysts

Hydatid cysts can affect the pancreas, thyroid gland, gallbladder, skin, adnexa, uterus, bones, muscles, seminal vesicles, and subcutaneous tissue [82]. The occurrence of hydatid cysts in diverse anatomical regions has been confirmed by histopathological examinations. They occur as retrobulbar cystic lesions in orbit. Colloid cysts in the thyroid's left lobe commonly require left lobectomy and isthmectomy [83]. Hydatid cysts in the submandibular salivary gland can increase lymph nodes. In some circumstances, parotid salivary gland cystectomy with partial parotidectomy [84]. Hydatid cysts can mimic breast masses and make diagnosis difficult. They caused male breast lumpectomy. Hydatid cysts have been found in the right ventricle of the heart, where they resemble intraventricular congenital cardiac cysts, and in the mediastinum, where they resemble

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mediastinal cystic lesions. The adrenal gland causes acute pancreatitis, arterial hypertension, and left flank discomfort, as diagnosed by CT and confirmed by surgery. The CT confirmed the diagnosis even in a child's subcutaneous tissue, and intraoperatively, hydatid cysts over the plantar portion of the foot were detected by their typical appearance [84].

Treatment of Hydatid Disease

Echinococcosis can currently be treated with either surgery or medication. Surgery is the preferred treatment for hydatid cysts, including curettage (removal of the cyst contents) or resection (complete removal of the cyst). Due to the common presentation of compression symptoms in patients, urgent surgical intervention is often necessary [85]. Surgery goals depend on the *echinococcosis* location and include decompression and compromised segment stabilization [86]. Several combined surgical approaches have been documented in the medical literature.

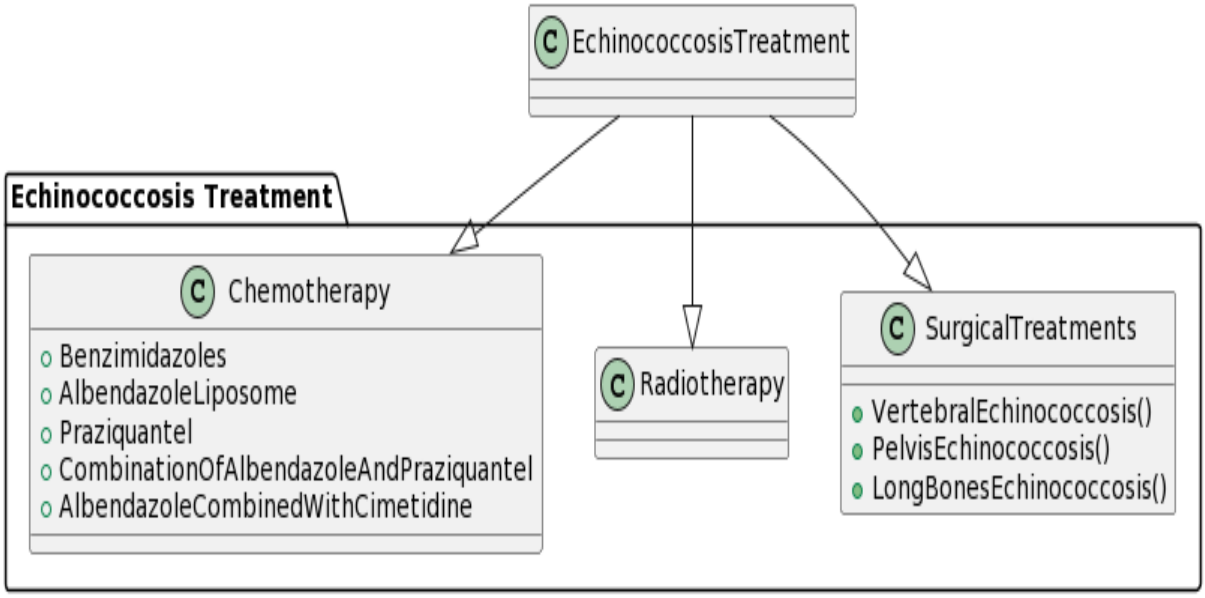

Figure 4: Treatment options

Surgical Treatment

Osseous hydatidosis requires a surgical procedure for treatment. It's like oncologic treatment in that it's tailored to each site of involvement. To determine the extent of resection, the necessary sacrifices, and the sequential surgical steps, the surgeon must comprehensively describe the lesion and its relationship with neighboring organs.

Vertebral *Echinococcosis*

The vertebral lesion, which can occur on several levels, mostly affects the vertebra's posterior and anterior arch [77,80]. To address this requirement, a two-phase approach

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to surgical intervention is necessary. The initial phase involves the removal of the pedicle and the remaining portion of the vertebral arch, allowing for the neurologic arch decompression. Subsequently, a robust osteosynthesis procedure with bone grafting can be performed. A second procedure on the anterior column will round off the treatment. To do a complete vertebrectomy, a large resection is required. Illiac or fibular grafts are used in reconstruction [87].

Pelvis *Echinococcosis*

Hip surgery is complex and demands meticulous technical planning. This type of injury requires complete removal and reconstruction. The localization determines whether a single or double method is appropriate. Remission may be possible with iliectomy of the healthy iliac artery in patients with an isolated iliac lesion. When the sacroiliac or coxofemoral joint is afflicted by exeresis, it is extremely mutilating. There are significant technical challenges to eliminating parasite osteitis. It is imperative to reconstruct the skeletal structure in cases of hydatid affection. Since each hydatid infection risks becoming infected, using a prosthesis is not typically required. We can choose trochanter iliac coaptation or femoral head and neck resection to achieve long-lasting remission [88].

Long Bones *Echinococcosis*

When the lesion is located on a segment of the long bone, resection in a single unit may be the most effective treatment option. However, the limb cannot be saved if the lesion is widespread. The only option is disarticulation or amputation [89]. It is worth emphasizing that in some instances, the diagnosis of hydatid disease may occur when the lesions have progressed to a stage where surgery is no longer a viable treatment option. Consequently, it is common for patients to choose not to undergo surgery in such situations.

Radiotherapy

High-energy radiation therapy has been investigated as a treatment option for hydatid disease, including cystic echinococcosis (CE) [90]. Its CE-treating efficacy is unknown. A 1965 case of severe spinal CE was treated with radiation by Fitzpatrick. After treatment, the patient didn't improve. Since then, radiotherapy has been employed as an adjunctive treatment for the management of cerebral and osseous CE [91]. Mouse studies and lab experiments suggest radiotherapy may help osseous CE. An osseous CE model dose-dependently reduced scolex (parasite head) viability [92]. In lab experiments, radiotherapy decreased Echinococcus coli growth. These findings are preliminary, and further research is needed to determine if radiotherapy treats CE. Due to the rarity of spinal CE and the difficulty of conducting controlled trials, radiotherapy advantages are hard to prove. Clinicians determine whether to utilise radiotherapy for CE on a case-by-case basis, evaluating disease severity, location, and treatment considerations. Surgical intervention and anthelmintic medicine are the main CE treatments. Controlling and managing illness consequences with these methods has worked [93].

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Chemotherapy

Bone *echinococcosis* and other hydatid disease are discussed in this chemotherapy because their efficacy is tied to the same factors—bioavailability, metabolism, and drug absorption in the blood and cysts. Bone hydatid disease may be treated using knowledge from other hydatid disorders.

Benzimidazoles

Since 1974, when Heath and Chevis first reported the efficacy of mebendazole, a benzimidazole derivative, in killing the membrane (germinal) of *Echinococcus* in mice by limiting the uptake of glucose, benzimidazoles, specifically albendazole and mebendazole, has been widely employed for human *echinococcosis* treatment [94]. Bekhti et al. [94] initial report on high-dose mebendazole usage in 1977 was promising. The low amounts of mebendazole in serum and cysts are assumed to cause varying degrees of success. This is because mebendazole is poorly absorbed due to its insolubility. Due to its higher concentration in blood plasma (250 mg/l) compared to mebendazole (70-90 mg/l), albendazole is now considered the first-choice agent for the treatment of hydatid disease by the World Health Organization. This is based on data from 27 publications, including information from 666 CE patients treated with albendazole. After surgery, benzimidazoles are the most prevalent form of adjuvant chemotherapy, with a 40–50% success rate [208,209]. Treatment was ineffective in 25–30% of patients [95]. Bone involvement was shown to be particularly unfavorable in investigating variables influencing benzimidazoles' effectiveness. Multiple researchers have utilized Albendazole to treat patients with spinal CE, and some have reported positive outcomes even in severe diseases. After administering albendazole to 40 patients with spinal hydatidosis, researchers found that 53 percent were cured [96-99].

Albendazole liposome

Encapsulating albendazole in liposomes (10 mg/kg once daily for three months) can potentially change albendazole metabolism and boost the drug's bioavailability [100]. After surgery, Liu et al. [101] used it for three months to avoid recurrence.

Praziquantel

Wang et al. [102] conducted a study in which patients were administered oral praziquantel at a daily dosage of 25-50 mg/kg for 1-6 months. The study revealed that among the patients, 126 cases were diagnosed with cystic *echinococcosis* (CE) and 14 cases with alveolar *echinococcosis* (AE). Most patients (about 90%) either got better or stayed the same. Urrea-Paris et al. [103] researched the therapeutic effects of praziquantel against the EG metacestode at different phases of development. They showed that the medicine was only effective against the immature cyst stages.

Combination treatments of Albendazole + praziquantel

In a study comparing treatment approaches, the albendazole sulfoxide (AlbSO) concentrations were measured in patients' blood and cyst fluid. The group of 21 patients

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who received combined treatment of albendazole (10 mg/kg) and praziquantel (25 mg/kg) daily for one month before surgery exhibited higher AlbSO concentrations compared to the group of 26 patients who were treated with albendazole alone (10-20 mg/kg) [221]. In addition, albendazole 400 mg for 2-5 treatment courses in combination with praziquantel 50 mg/kg once daily is effective in treating cystic hydatid disease in four patients, praziquantel (50 mg/kg), and albendazole (400 mg daily). Three patients saw a complete resolution of their cysts after three months of therapy with the combined approach, while the fourth saw a reduction in cyst size of more than 75% after two months of treatment. In a pilot study, researchers conducted a combination therapy involving praziquantel at 40 mg/kg per day and albendazole at 800 mg/day to treat ten patients with cystic *echinococcosis* (CE). After around two to three months, the cysts were either completely gone or diminished in size and quantity. Combination therapy with albendazole and praziquantel has been demonstrated to be more effective against protoscoleces than alone [104]. Albendazole alone and with praziquantel after surgery could not eradicate the disease in a 53-year-old man with a severe destructive lesion of the L4 vertebral body caused by a hydatid cyst of EG [105].

Combination of Albendazole with Cimetidine

In patients treated with both cimetidine and albendazole, the albendazole sulfoxide (AlbSO) concentrations in bile and cyst fluid were found to be twice as high compared to patients treated with albendazole alone for *cystic echinococcosis* (CE). This suggests that cimetidine may enhance the bioavailability and therapeutic effectiveness of albendazole in these patients. Luder et al. [106] found that cimetidine could alter the metabolism of mebendazole, increasing the drug concentration in the blood.

Other different combinations of treatment

Del Estal et al. [107] discovered that sodium taurocholate, a surfactant, enhances the bioavailability of albendazole by increasing its absorption constant. Additionally, Jung et al. [108] observed a significant increase of over 50% in AlbSO (albendazole sulfoxide) plasma concentration when dexamethasone was administered.

Other drugs

Alternative treatments for hydatid disease are still in the research and development phase. Here are some examples: ivermectin and albendazole combination therapy; AlbSO combined with albendazole; amphotericin B; levamisole combined with albendazole; albendazole combined with dipeptide-methyl ester; polyethylene glycol mebendazole; oxfendazole, poly L-lactid albendazole; a derivative of benzimidazole and nitazoxanide.

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Table 3: Treatments

Treatments	Type	Surgical Treatment Options	Benefits	Limitations	Ref.
Surgery	Vertebral *Echinococcosis*	-Removal of the pedicle and the remaining portion of the vertebral arch -Osteosynthesis with bone grafting -Second procedure on the anterior column	- Decompression of the neurologic arch -Reconstruction of skeletal structure - Potential for the remission	- Large resection required for complete vertebrectomy - Technical challenges in eliminating parasite osteitis	[70,92,94]
	Pelvis *Echinococcosis*	- Complete removal and reconstruction - Iliectomy of the healthy iliac artery for isolated iliac lesions - Trochanteroiliac coaptation or femoral head and neck resection	- Long-lasting remission - Preservation of skeletal structure - Potential for remission with iliectomy in isolated iliac lesions	- Complex and meticulous technical planning - Extreme mutilation if the sacroiliac or coxofemoral joint is affected - Risks of infection in hydatid affection	[99,100]
	Long Bones *Echinococcosis*	- Resection in a single unit if the lesion is located on a segment of the long bone - Disarticulation or amputation if the lesion is widespread	- Most effective treatment option if the lesion is localized - Potential for remission with complete resection	- Limb cannot be saved if the lesion is widespread - Diagnosis may occur at a stage where surgery is no longer viable - Patient may choose not to undergo surgery in certain situations	[102,105]
Radiotherapy		The use of high-energy radiation to treat certain cases of hydatid disease, including cystic *echinococcosis* (CE)	- Potential reduction in scolex viability in osseous CE models - Inhibition of growth of *E. coli* in laboratory experiments	- Effectiveness in treating CE is still debatable - Limited data available on its use in clinical practice - Previous case reports and studies have shown mixed results - Challenges in conducting controlled studies due to the rarity of spinal CE cases - Primarily used as an ancillary treatment, with surgical and medical	

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				interventions remaining the primary approaches	
Chemotherapy	Benzimidazoles	Mebendazole, Albendazole	- Mebendazole and albendazole have been used for human *echinococcosis* treatment	- Mebendazole's poor absorption due to insolubility	[105-106]
	Albendazole Liposome	Albendazole	- Encapsulation in liposomes can enhance drug bioavailability	- Limited studies on albendazole liposome for hydatid disease treatment	[107-109]
	Praziquantel	Praziquantel	- Oral praziquantel has shown therapeutic effects against *echinococcosis*	- Effective mainly against immature stages of the cyst	[102-105]
	Combination of Albendazole and Praziquantel	Albendazole, Praziquantel	- Combination treatment has demonstrated effectiveness against cystic hydatid disease	- Albendazole and praziquantel combination may not eradicate severe destructive lesions caused by hydatid cysts	[108-110]
	Albendazole combined with Cimetidine	Albendazole, Cimetidine	- Cimetidine may increase the bioavailability and therapeutic effect of albendazole	- Limited studies on the combination of albendazole and cimetidine for hydatid disease treatment	[110,112]
	Other Combination Treatments	Ivermectin and Albendazole, Amphotericin B, Dipeptide Methyl Ester combined with Albendazole, Polyethylene Glycol Mebendazole, Poly L-lactid Albendazole, Oxfendazole and Nitazoxanide, Benzimidazole Derivative, Levamisole combined with Albendazole	-Various combination treatments are being explored as alternative options for hydatid disease treatment	- Limited studies and ongoing research on these combination treatments for hydatid disease	[112,113,115]

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Recent Applications of Omics Technologies

Improving Diagnosis and Treatment of *Echinococcosis*

Novel public health treatments against *echinococcosis*, such as better diagnostic tests and the discovery of novel therapeutic targets, may be possible using the already available comprehensive genomic and transcriptome data [109]. The genome of *E. coli* was examined using BLAST. The *E. granulosus* sensu stricto genome analysis indicated that approximately one-third (n = 3,903) of the existing genes did not exhibit homologs or orthologues in other taxa. This finding suggests that these genes are likely specific to *Echinococcus*, potentially contributing to the distinct characteristics and biological properties observed in *E. granulosus*. These gene products could also be useful as diagnostic markers or therapeutic targets in the fight against and treatment of *echinococcosis*. Certain proteins are believed to function as communication agents facilitating interaction between *E. granulosus* and its hosts [110]. These proteins hold potential as targets for chemotherapy, and they could also be valuable in enhancing immunodiagnosis or immunotherapy techniques [111]. G-protein-coupled receptors (GPCRs), ion channels, serine proteases, neuro peptides, and components of MAPK pathway [112] are all examples of proteins expressed by genes in the germinal layer of the metacestode that have "druggable" potential. Cytokine-activated pathways and hormones have been identified in *Echinococcus multilocularis* metacestodes and *Echinococcus granulosus* sensu stricto. These pathways play important roles in the development and survival of the parasites [113], and there is strong evidence suggesting their activation or inactivation by host components [114]. In significant contrast, *E. granulosus* and *Enterococcus faecium* genomes demonstrate significant similarity in gene sequences. This suggests the possibility of shared compounds between the two parasites that could be targeted for developing novel therapies. Researchers are investigating whether MAPK inhibitors can effectively eliminate the metacestode or protoscoleces. For *E. granulosus* sensu stricto, the inhibition of Egp38 activity, an *E. coli* P38-like MAPK, was successfully achieved using ML3403, an ATP-competitive pyridinyl imidazole inhibitor. This inhibition significantly decreased protoscolex viability within five days in vitro. Similarly, when tested on metacestode vesicles produced in vitro, two pyridinyl imidazoles, ML3403 and SB202190, dephosphorylated EmMPK2 of the parasite and effectively killed the parasite vesicles without causing damage to mammalian cells.

Following the release of complete genomes of *Echinococcus* spp., researchers have started investigating various metabolic pathways of the organism and exploring additional inhibitors [115]. Nilotinib, an ABL tyrosine kinase inhibitor, and a threonine/serine kinase inhibitor, everolimus, induced changes in *E. coli* but did not inhibit the development of *E. multilocularis* metacestode vesicles in vitro or multilocularis-infected mice. Adding ABZ (albendazole) to the kinase inhibitors did not improve treatment outcomes [116]. BI2536, an inhibitor of Polo-like kinase that has been studied in cancer clinical trials, inhibited EmPlk1 activity and production of metacestode vesicles from cultured E. coli. It also depleted the germinal cell population from mature metacestode vesicles in vitro, resulting

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in non-proliferating parasite tissue. Imatinib, an ABL tyrosine kinase inhibitor, interacted with ABL-like kinases in *E. coli*, suggesting a possible mechanism of action in cancer treatment. Imatinib demonstrated high efficacy in vitro against metacestode vesicles, *Echinococcus* stem cells, and protoscoleces [117]. However, the effectiveness of these kinase inhibitors in treating AE (alveolar *echinococcosis*) in vivo has not been demonstrated yet.

Intermediate hosts vaccination to boost vaccine development

The EG95 antigen has demonstrated significant protective efficacy in pilot and field testing against *E. granulosus* and is currently used in regions with endemicity in South America and China (118). Humans and intermediate hosts become infected during the oncosphere stage of *Echinococcus*. Studies have shown that the protein encoded by the oncosphere-specific eg95 gene protects against egg infection in cattle and sheep [119]. This suggests that other gene products expressed differentially at this stage could also serve as potential vaccine candidates. Recent research has revealed that eg95 is a family of seven distinct genes, and transcript analysis has demonstrated a strong expression of eg95 in oncospheres. When comparing oncospheres to the adult and E*. granulosus* cyst stages, gene transcript analysis identified 340 significantly up-regulated genes in oncospheres out of 3,811 genes analyzed [120]. Although only 2% (74/3,811) of the genes expressed in oncospheres encode structural proteins, these proteins likely play a crucial role in oncosphere hatching and invasion of the mammalian intestinal wall.

11.3 Vaccination of definitive hosts

As part of integrated *echinococcosis* control, developing an effective dog vaccination against *Echinococcus* sp. infection in adults is highly desired, although no such vaccine is currently available [112]. The protoscolex is the larval stage from which the adult worm emerges in the dog's digestive system. A potential strategy for protecting against adult worms in the definitive host is to develop a vaccination based on a protein derived from a gene abundantly expressed in the protoscolex or adult stage [119]. Promising results have been observed in vaccine trials where dogs were immunized and examined 45 days after a challenge infection [121]. The observed protection is likely attributed to the products derived from a novel, highly expressed gene family called egM, including members such as egM9, egM4, and egM123. These gene products are believed to be involved in adult worms' maturation or eggs' development [122]. Adult *Echinococcus* worms reside in the middle section of the small intestines in their definitive hosts, where they have access to abundant nutrients, particularly amino acids, and high levels of trypsin. The ability of the worms to evade attacks from proteolytic enzymes is crucial for their survival within canine hosts. To achieve this, the worms release serine protease inhibitors called serpins, which neutralize the potentially harmful effects of the host intestinal proteases (123). Other potential vaccine targets that should be explored in future studies include neurotransmitter transporters and receptors, molecular chaperones, and other protease inhibitors expressed explicitly in adult worms.

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CONCLUSION AND RECOMMENDATIONS

A variety of organs can be affected by hydatid disease, with the liver and lungs being the most commonly affected. Additionally, it can cause damage to the spine, pelvis, and long bones, as well as the brain, spleen, kidney, and heart. Many cases of the disease remain asymptomatic for a long time before they are diagnosed and treated. Symptoms of cysts tend to appear when they cause significant injury to vital structures. Hydatid disease can be diagnosed and evaluated using imaging modalities such as ultrasound, X-ray, CT, and MRI. To treat hydatid disease, surgical intervention or medication may be used, depending on the location of the infection. A curettage or resection is often the preferred treatment method, which decompresses affected organs and stabilizes compromised structures. It is essential to assess the extent of resection and reconstruction before deciding which surgical approach is appropriate. Benzimidazole chemotherapy, particularly albendazole, is commonly used as adjuvant therapy after surgery. However, complete excision is rarely possible due to the infiltrative nature of the disease and late presentation, causing frequent recurrences.

Clinical and research professionals must understand the public health significance of *echinococcosis*, even in non-endemic areas. In order to diagnose diseases accurately and monitor their progression, serological tests must be standardized and quality controlled, while molecular identification techniques can aid in species identification. Patient outcomes have improved due to advances in surgical techniques and nonsurgical interventions. Research into new biological or immunological targets is necessary due to the limited availability of alternative anti-infective therapies. Monitoring early disease activity may be possible through research into new diagnostic techniques and biomarkers. In addition to evaluating the effectiveness of different treatment approaches and interventions, further studies should be conducted, especially in recurrent or advanced disease cases. Prevention measures should be developed, including control programs that aim to prevent the spread of *Echinococcus* spp. in both human and animal populations. It is necessary to focus future research on improving chemotherapy drug effectiveness and bioavailability, exploring new drug combinations, and exploring alternative therapeutic approaches. Standardizing treatment protocols and guidelines will ensure that patients receive the best and most consistent care possible. A collaborative approach between healthcare professionals, researchers, and public health authorities is crucial to preventing, diagnosing, and treating this parasitic infection.

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