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Cystic Echincoccoosis: A Comprehensive Review on Life Cycle, Epidemiology, Pathogenesis, Clinical Spectrum, Diagnosis, Public Health and Economic Implications, Treatment, and Control

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Abstract

The larval (metacestode) stage of cestodes belonging to the genus *Echinococcus*, family *Taeniidae*, causes echinococcosis, which is one of the most serious tropical helminthic infections of livestock with financial and public health implications in both developed and developing countries. The larval stage of *Echinococcus granulosus* causes cystic echinococcosis (CE), a serious zoonosis. Cystic echinococcosis causes significant economic loss in farm animals due to the condemnation of edible organs, decreased meat and milk output, lower hide and fleece value, and decreased reproduction. In humans, economic loss refers to monetary losses incurred as a result of diagnosis, hospitalization, surgical intervention, or percutaneous therapies. Treatments, post-treatment care, and travel for patients and family members, as well as indirect costs, such as mortality and suffering. With the exception of Antarctica and nations where echinococcosis has been eradicated by extensive control efforts, such as Iceland, New Zealand, Tasmania, and the Falkland Islands, it is associated with substantial economic losses and public health significance globally. Carnivores are well-known for being terrific hosts. The infection occurs when humans consume parasite eggs found in the contaminated food, drink, or soil, or when they come into direct contact with animal hosts. Specific control measures include stray-dog control, registration of all owned dogs, spaying of bitches, and praziquantel medication of all (or most) dogs at predetermined intervals (such as every 6 or 8 weeks), strict meat inspection, proper disposal of affected viscera of food animals, and health education.

Keywords

Echinococcus granulosus, Economic significance, Echinococcosis, Helminthic zoonosis, Public health importance

1. Introduction

Echinococcosis, commonly known as hydatidosis, hydatid disease, is a serious problem for domestic animals and a zoonotic disease that causes significant economic losses and public health issues around the world [1]. Because humans serve as an unintentional intermediary, hence, echinococcosis is significant from public health point of view [2]. It is one of the most underappreciated tropical parasite diseases of livestock, with monetary and public health implications [3, 4]. Cystic echinococcosis is caused by the cestode/flatworm *E. granulosus*, which belongs to the genus *Echinococcus* and the family *Taeniidae*, in its adult or larval (metacestode) stages. The zoonotic pathogen *E. granulosus* is found all over the world [5]. It is one of the most widely distributed parasitic zoonoses, with a global distribution. *Echinococcus granulosus* (which causes hydatidosis), *E. vogeli*, and *E. oligarthrus* (which produce polycystic echinococcosis), and *E.multilocularis* (which causes alveolar echinococcosis/AE/) are the six species of *Echinococcus* that have been identified so far. *Echinococcus felidis* and *E. shiquicus* have also identified from African lions and Tibetan foxes. However, their zoonotic transmission potential to humans is yet unknown [6, 7].

The parasite *Echinococcus granulosus* feeds on canids, which are its primary hosts in the small intestine [8]. For the parasitic larval stage, domestic ungulates serve as intermediate hosts (metacestode). *Echinococcus granulosus* cysts typically form in the host's liver or lungs [9]. Hydatid disease in ruminant animals, hydatidosis in humans, and echinococcosis in canines are all documented symptoms of this parasite [10]. Until the helminthic larva reaches a specific size, it remains latent; and clinical signs do not arise. Nonetheless, this parasite is found around the world, although it is more common in rural places where sheep and goats are still slaughtered in the traditional manner and corpse wastes are readily available to scavenging dogs and other wild carnivores [11].

Echinococcosis is a silent cyclo-zoonotic illness that causes severe morbidity and mortality in humans and herbivore animals [12]. The larval stage of *E. granulosus* has a complicated life cycle that alternates between definitive carnivore hosts like dogs and other canids and intermediate hosts including cattle, pigs, buffaloes, camels, sheep, and goats [13, 14]. Factors affecting the prevalence or status of echinococcosis are determined on a local level and are linked to current social, cultural, environmental, and epidemiological conditions. The dynamics of transmission differ between the dog and its usual intermediate and human hosts, and human behavior plays a crucial influence in epidemiology of this cyclozoonosis [15].

Echinococcosis is still considered a neglected disease, despite the fact that it causes direct or indirect losses in both domestic animals and humans. Therefore, the objective of this paper is to present comprehensive review on echinococcosis with particular reference to life cycle, epidemiology, pathogenesis, clinical spectrum, diagnosis, public health and economic implications, treatment, and control.

2. Etiology and Taxonomy

The etiological agent cystic echinococcosis is *Echinococcus granulosus*, a tiny carnivorous tapeworm. It is a parasitic zoonotic disease produced by the larval stage (metacestode) of *Platyhelminthes*, Class *Cestode*, Order *Cyclophyllidea*, family *Taeniidae*, and genus *Echinococcus* [16].

2.1. Morphology of Echinococcus

The adult *E. granulosus* has a lucky streak. It's a tiny worm with a length of 2 to 9 mm. It has three or four segments, a globular scolex with a rostellum and four cuplike oval suckers, and a globular scolex of 0.3 mm in diameter (Figure 1) [17]. A double crown of big and small hooklets adorns the rostellum. Most protoscoleces contain two rows of hooks, with an equal number of large and small hooks on each row. A short neck and one or two immature segments follow the scolex. Testes and ovaries have completely formed reproductive organs in the mature segment. The gravid segment is the widest and longest of the three. The uterus in the gravid unit can hold up to 500 eggs, which are released into the feces through the ruptured segment. The subspherical egg is 34 to 41m in diameter, with a brown hexacanth embryo, and resembles those of other *Taenia* worms in appearance [18].

3. Forms of Echinococcosis in Animals

The four species of the genus *Echinococcus* infect several carnivore species as definitive hosts, causing echinococcosis in the intestine. *Echinococcus* species develop metacestode stages in the internal organs, primarily viscera, of natural intermediate hosts and, on rare occasions, in aberrant or accidental hosts. Table 1 shows many kinds of echinococcosis in animals [20].

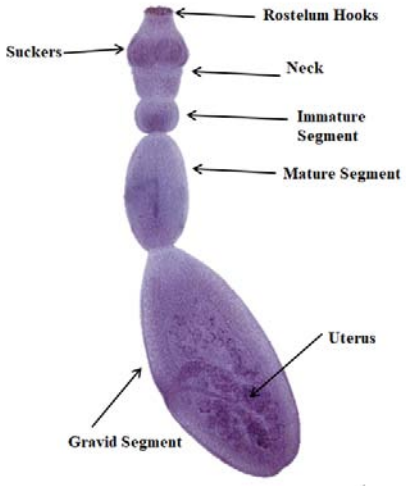

Figure 1. Morphology of adult worm of *Echinococcus granulosus* Source [19].

Table 1. Different species and forms of echinococcosis in animals

Stage of *Echinococcus* species	Form of echinococcosis	Animal hosts involved
E. granulosus	Intestinal echinococcosis	Exclusively definitive hosts metacestode stage
	Cystic echinococcosis (CE)	Intermediate and aberrant hosts, rarely definitive hosts
E. multilocularis	Alveolar echinococcosis (AE)	Intermediate and aberrant hosts, rarely definitive hosts
E. vogeli	Polycystic echinococcosis (PE)	Intermediate hosts
E. oligarthrus	Polycystic echinococcosis (PE)	Intermediate hosts

4. Life Cycle of *Echinococcus*

The life cycles of *E. granulosus* (Figure 2) can be classified as domestic, with the domestic dog serving as the main definitive host and various species of domestic ungulates serving as intermediate hosts, or sylvatic, with wild carnivores (foxes, wolves) and Cervidae (elk; alces, reindeer; *Rangifer tarandus* and red deer; *Cervus elaphus*) serving as hosts; the sylvatic [21]. Domestic and sylvatic life cycles coexist or overlap in many endemic infection locations [22].

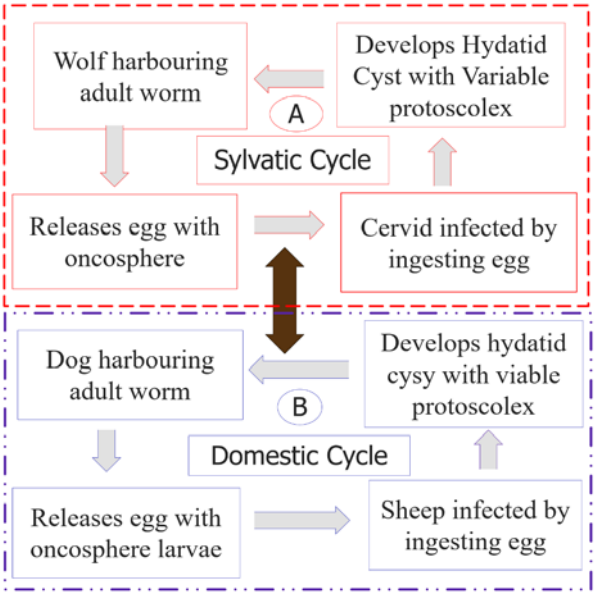

Figure 2. Interaction between sylvatic cycle and the domestic cycle of *E. granulosus* (indicated by bidirectional arrow) [23].

For *Echinococcus* spp. to complete its life cycle, it needs two mammalian hosts. The adult tapeworm can be discovered in the definitive host's small intestine, where segments bearing eggs are passed along with the feces. The oncospheres enter the small intestinal wall when the eggs are consumed by intermediate hosts such as cattle, sheep, goats, pigs, and camels, in which the metacestode develops. The penetration of the oncospheres into the intestine is aided by a hormonal discharge from the oncospheres.

The oncosphere are passively transported to the liver, where some are retained, others reach the lungs, and a few may be transported to the kidney, spleen, muscles, brain, and other visceral organs after gaining access to a venue [24].

Once the oncospheres have arrived at their final destination, the metacestode stage begins. Over the course of several months, the hydatid cyst forms an outer laminated membrane known as the germinal layer. Brood capsules form from the germinal membrane, each containing one or more invaginatinated head (protoscolices) that can grow into the adult tapeworm when consumed by the definitive host [25]. The protoscoleces evaginate after ingestion adhere to the intestinal mucosa, and mature into adult stages in 32 to 80 days [26]. The detailed life cycle of cystic echinococcosis is presented in Figure 3.

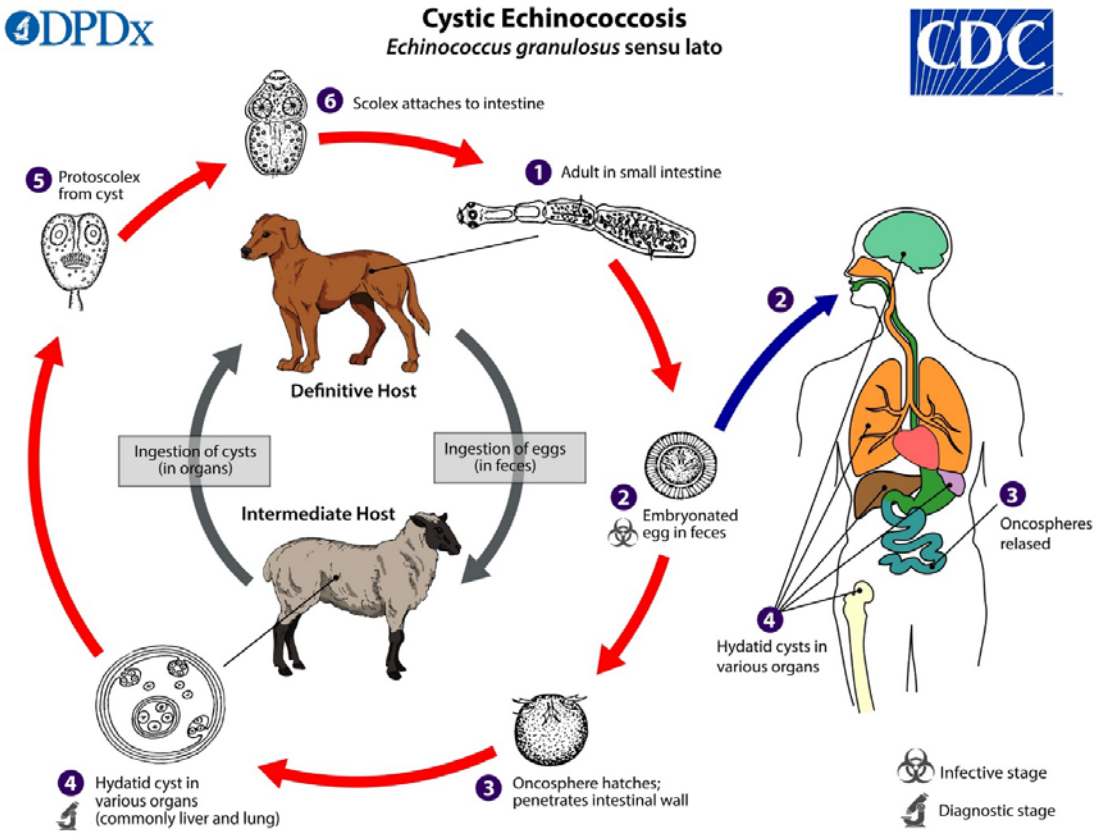

Figure 3. Life cycle of cystic chinococcosis [27].

5. Epidemiology

Epidemiology is the study (scientific, systematic, and data-driven) of the distribution (frequency, pattern) and determinants (causes, risk factors) of health-related states and events (not just diseases) in defined populations (neighborhood, school, city, state, country, global) or branch of medical science concerned with disease transmission and control [28].

5.1. Geographic Distribution

Cystic echinococcosis is found all over the world, and in some areas, it is a major economic and public health issue [29]. Cystic echinococcosis is not found in Antarctica and has been eradicated in Iceland, New Zealand, Tasmania, the Falkland Islands, and Cyprus thanks to comprehensive control programs. In sheep-raising areas of the

Mediterranean, Australia, Eastern Africa, South America, and the Middle East, including Saudi Arabia, hydatidosis caused by *E. granulosus* is common [30].

In regions of China, Central Asia, Eastern Europe, and Israel, there is clear evidence for the rise or re-emergence of human cystic chinococcosis. The highest incidences of infection are found in communities where the sheep are raised [31, 32].

5.2. Mode of Transmission

Primary cystic chinococcosis infections are acquired by humans through oral uptake of *E. granulosus* eggs shed by the infected dogs or other animals [33]. Handling diseased definitive hosts, egg-containing excrement, or egg-contaminated plants or soil, followed by direct hand-to-mouth transmission, can all lead to infection. Wind, birds, beetles, and flies can contaminate food, drinking water, and surfaces with *Echinococcus* eggs, making them a possible source of infection for humans and cattle [20, 34, 35].

Cystic chinococcosis is transmitted to intermediate hosts by consuming the tiny eggs while grazing on polluted pastures with dog excrement. The definitive hosts are infected by ingesting infected cysts containing organs that have been condemned at abattoirs [36, 37].

6. Pathogenesis

6.1. Echinococcosis in Definitive Hosts

Echinococcus parasites penetrate deeply between the villi into the Lieberkühn crypts of the small intestine, adhering to the epithelium with suckers and rostellar hooks. Normally, this close parasite-host connection does not result in severe pathology. Minor alterations such as epithelial cell flattening, cellular infiltration of the mucosa, and increased mucus production may occur. The parasite's scolex area releases excretory/secretory products, which may cause the development of circulating antibodies. Except in huge numbers, which can cause severe enteritis, the adult tapeworm is neither harmful nor fairly harmless to dogs [22].

6.2. Cystic Echinococcosis in Intermediate Hosts

The majority of cysts were spherical and varied in size. They were either bulging from the surface or discovered deep into the parenchyma of the lungs or liver. The cyst had a thick membrane and cavities lined by a smooth membrane that could be easily removed on the sliced surface. Others were calcified and filled with a clear or turbid fluid, caseated (cheese-like) substance, or both [38].

The effect on the host is determined by the parasitized organ and the size of the hydatid cyst, which can grow to be several inches long. Mononuclear cells, eosinophils, multinucleated giant cells, and fibrous connective tissue frequently surround the hydatids. When the cyst ruptures, the inflammatory response becomes more severe. In humans, the rupture of the cyst can cause anaphylactic shock or other severe allergic reactions, as well as compressive atrophy of the surrounding tissues. Hydatid cysts can deteriorate without warning, resulting in calcification [39].

6.3. Cystic Echinococcosis in Humans

Hydatid cysts of *E. granulosus* develop primarily in the liver and lungs as unilocular fluid-filled bladders in humans, as they do in herbivorous intermediate hosts, but they can also develop in almost any internal organ or tissue (heart, bone, muscle, nervous system) via hematogenous dissemination, or in the abdominal cavity [16, 40].

Most primary infections in humans result in a single hydatid cyst; however, 20 percent to 40 percent of cases have multiple cysts or multiple organ involvement, suggesting that many eggs of *E. granulosus* were consumed by the same patient [41, 42]. Human hydatid cysts caused by *E. granulosus* infection was reported as fertile, sterile, and calcified cysts in the human liver and lungs.

7. Clinical Symptoms

In domestic animals, hydatid cysts in the liver or lungs are normally tolerated without causing any clinical indications, but the majority of hydatid cysts in the liver or lungs cause minimal visible damage, and their presence is only revealed at abattoirs [43]. However, the clinical manifestation of the disease in symptomatic cases varies greatly depending on the organ involved, the size of the cyst and its location in relation to the involved organ, the interaction between the expanding cysts and the adjacent organ, and complications caused by cyst rupture [24, 44].

Clinical signs can appear months or years after a highly variable incubation period in humans. The cysts in the liver can be asymptomatic for 10-12 years. However, they can cause upper abdominal pain, cholestasis, hepatomegaly, biliary cirrhosis, portal hypertension, ascites, and other symptoms. The majority of persons with echinococcosis, especially in the early stages, are asymptomatic [45]. The most common symptoms of cerebral hydatid cysts are headache and vomiting due to increased intracranial pressure; other symptoms include seizures, visual abnormalities, and ataxia [46].

If the cysts become large enough, they can cause a variety of symptoms, including abdominal pain and mass, cholestasis, obstructive jaundice, biliary duct dilatation, and the creation of a fistula in cases of hepatic cystic chinococcosis. Fever, thoracic discomfort, dyspnea, chronic cough, and bloody sputum are some of the most prevalent symptoms in patients with pulmonary cystic echinococcosis. For patients with liver echinococcosis, hepatomegaly is the most common symptom [47]. Bone cystic echinococoosis is generally asymptomatic for a long time, and is only discovered after a sudden fracture [41].

8. Diagnosis

8.1. Diagnosis in Intermediate Hosts

The most reliable diagnostic approach in the intermediate host is cyst identification during meat inspection at post-mortem examination. As a result, the presence of hydatid cysts in internal organs is a critical diagnostic tool for confirming the condition [20].

8.2. Diagnosis in Definitive Host

Adult tapeworm infection in dogs is difficult to diagnose since the segments are tiny and only shed sparingly [48]. Microscopic egg detection in fecal samples cannot be used to diagnose *E. granulosus* infection because these eggs are morphologically identical from those of *Taenia* species [49]. An egg can be found in fecal samples using the standard flotation technique, or on the perineal skin using clear adhesive tape that is pushed to the skin, transferred to a microscopic slide, and studied. If in good condition, Proglottids of *E. granulosus* spontaneously expelled by dogs and identified predominantly on the surface of fecal samples may allow a proper morphological diagnosis [48].

8.3. Diagnosis in Humans

In people, the diagnosis is confirmed by imaging (computer tomography (CT), X-rays) and identification of the typical or worrisome cyst structure [50]. Cysts are diagnosed using imaging techniques such as CT scans, ultrasonography, and magnetic resonance imaging (MRI), and once a cyst is found, serological testing may be utilized to confirm the diagnosis in humans [44].

9. Public Health Importance of Echinococcosis

Cystic chinococcosis in humans is an infection produced by the larval stage, the metacestode of *Echinococcus* species, and can range from asymptomatic to severe disease that can be fatal. It is a significant public health issue in certain nations, and it may be emerging or reemerging in others. Worldwide, it is estimated that approximately 2-3 million human cases occur. The most frequent type of the disease in humans and domesticated animals is cystic echinococcosis, which is caused by *Echinococcus granulosus* sensu lato [51, 52].

Following primary infection, *Echinococcus granulosus* may block several anatomic locations. The majority of hydatid cysts are found in the liver (70%) or lungs (20%). However they can also be found in other organs (kidney 2%, spleen 2%, and brain less than 2%) [53]. The hydatid cyst causes severe sickness and death in people, as well as economic losses due to treatment costs, lost wages, and cattle annual production losses [54].

Mechanical malfunction of organs caused by cysts, as well as anaphylaxis as a result of the cyst breach and discharging fluid, are significant manifestations in humans. The development of cysts containing several microscopic protoscoleces, which most commonly occur in the visceral organs, central nervous system, and skeletal system, as well as thyroid glands, subcutaneous tissues, body cavity, and musculature, characterizes hydatidosis [55]. The incubation period for all *Echinococcus* species ranges from months to years or even decades. It is mostly determined by the size and rate of cyst growth in the body [56].

In humans, hydatid cysts are frequently fertile, and various studies suggest that the high number of cases could be related to increased infectivity or pathogenicity of *E. granulosus* sensu-lato. Unless other mechanical conse-

quences such as rupture, compression of critical structures, and hemorrhage occur, asymptomatic infection frequently predominates. This could be due to the parasite evading host immunity [57].

Although cystic chinococcosis is a potentially fatal condition, cysts are usually well tolerated unless they injure or burst nearby tissues. Many cysts are asymptomatic throughout a person's life and may be discovered by chance during surgery or autopsy. This type of echinococcosis is normally curable; nevertheless, some infections can be fatal if the cyst ruptures and produces anaphylactic shock or destroys essential organs. The outlook for symptomatic cysts in the brain, kidney, heart, or other important organs is bleak [58].

Tumor, hepatomegaly, cholestasis, jaundice, secondary biliary cirrhosis, biliary colic-like symptoms, liver abscess, calcified lesions in the liver, portal hypertension, and thrombosis can all result from the development of a hydatid cyst in the liver, lung, or other organs [59].

Lung tumor, chest pain, chronic cough, dyspnea, hemoptysis, pneumothorax, pleuritis, and lung abscess are all symptoms of a lung tumor. Pain, tumor, cardiac insufficiency, and embolism are all conditions that can occur in the heart. Pain, bone expansion, bone fragility, and muscle cysts are all symptoms of bone and muscle disease. Tumor in the brain and spine cause neurological symptoms and back pain. Pain, ptosis, and visual abnormalities in the eyes biliary colic, cholestatic jaundice, cholangitis, fever, pancreatitis, and allergy result from the cyst rupture in the liver to the biliary tree. Cyst rupture in the bronchial tree causes asthma-like symptoms such as coughing, dyspnea, and hemoptysis, as well as fever [60].

10. Economic Importance

Cystic echinococcosis is major economic problem in both humans and animals [61]. The immediate economic losses caused by hydatid cyst infection in animals result from the condemnation of carcasses and visceral organs, such as the liver, lungs, spleen, heart, and kidneys [33]. Furthermore, it causes retarded growth, decreased performance, decreased milk and meat yield, as well as decreased to poor quality wool, decreased hide and skin value, and decreased birth rate [52].

Many countries around the world suffer significant economic losses and public health difficulties as a result of echinococcosis, including Europe, Asia, Africa, South America, Canada, and Australia [33]. Many places have reported cystic and alveolar echinococcosis. However, cystic echinococcosis is more prevalent and has been reported from all countries in the Middle East and Arabic North Africa [62].

In humans, economic loss is associated with direct monetary loss as a result of diagnosis, hospitalization, surgical intervention, or percutaneous treatments. Therapies, post-treatment care, and travel for patients and family members, as well as additional indirect costs like as death and suffering. Aside from the economic and social effects of incapacity associated with undetected and thus untreated cases, the loss of working days or "output" and abandonment of farming or agricultural activities by affected or at-risk individuals must be considered. Furthermore, according to most reports, between 1% and 2% of cystic chinococcosis cases are deadly [18].

Even after accounting for human cystic chinococcosis underreporting, the disease has a significant worldwide impact in terms of disability adjusted life years (DALYs) and monetary costs. For example, the cost of human health treatment and livestock losses in North African countries was estimated to be US$ 60 million per year [33].

11. Treatment of Cystic Echinococcosis

Echinococcus tapeworms are more difficult to eradicate than other *Taenia*, although numerous extremely effective medicines, most notably praziquantel, are now available. Following treatment, it is recommended that dogs be confined for 48 hours to allow for the collection and disposal of contaminated feces. In humans, hydatid cysts can be surgically removed, although mebendazole, albendazole, and praziquantel therapy have been shown to be effective [43].

The treatment of cystic echinococcosis in humans is determined on the location and size of the hydatid cyst (s) in the body. In humans, the surgery is still the only reliable method of treating hydatid cysts, and chemotherapy, particularly albendazole, is indicated only when surgery is not an option. A combination of surgery and benzimidazole, mebendazole prevents protoscoleces from developing into hydatid cysts and keeps the cyst dry. Membrane collapse if the medicine was administered to the patient prior to surgery [63].

12. Prevention and Control

Because prevention is preferable to cure, it is preferable to prevent echinococcosis before it causes significant damage that necessitates additional expenses and efforts to remove. The disease is controlled by removing hydatid

tapeworms from dogs using the appropriate control procedures. The infection of dogs with tapeworms, as well as the spread of the disease to other animals, including humans, can be avoided [27]. Vaccinating sheep with an *E. granulosus* recombinant antigen (EG95) offers promising preventative and control potential. The abolition of sheep farm slaughter minimizes the possibility of canines becoming infected from this source [16].

Several *E. granulosus* control approaches have been thoroughly examined and are reported in detail elsewhere. One alternative (type I) stresses long-term public health education initiatives in conjunction with primary health care and veterinary public health activities, such as improved slaughter cleanliness and meat inspection, dog registration, and sanitation measures. Another alternative (type II) is based on legislation and involves particular measures designed to halt parasite transmission. Prior to the program's attack phase, baseline data is collected to serve as a reference for monitoring control progress [17].

Stray-dog control, registration of all owned dogs, spaying of bitches, and medication of all (or most) dogs with praziquantel at predetermined intervals, such as every 6 or 8 weeks, are all specific control measures. These steps are supplemented by improvements in meat inspection, abattoir hygiene, slaughter offal disposal, public health education, and other initiatives [64, 65]. Control efforts in several nations have demonstrated that the attack phase may be completed successfully in less than 15 years if the essential steps are carried out without substantial restraints and financial constraints [16].

13. Conclusion and Recommendations

Echinococcosis is one of the most serious helminthic zoonoses, and it is still a major problem around the world. The most common species are *E. granulosus* and *E. multilocularis* that have been reported from many nations. The ingestion is the principal mode of transmission; and the disease affects people of all ages, and both sexes. Furthermore, echinococcosis generates significant economic loss as well as substantial human health issues. Dogs are the definitive hosts of the parasite *E. granulosus*, which harbors the adult parasite and excretes parasite eggs with their feces, whereas animals and humans are intermediate hosts. Humans can become intermediate hosts by inadvertently consuming tapeworm eggs. This could indicate that the public health relevance of hydatidosis stems from eating tapeworm eggs. As a result, the disease necessitates strong community awareness in order to break down different channels of transmission. Further research is needed on the development of simple, sensitive and cheap diagnostic test that can be widely employed even by poor resource nations to confirm the disease at ante-mortem in various food animals that are subjected to slaughter in abattoirs.

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Contribution of Authors

During the writing of the manuscript, all of the authors contributed equally. They read the final manuscript and gave it their approval for publishing.

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