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Review Article

Zoonotic Importance of Echinococcosis and Strategies for Its Prevention and Control

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Abstract

Echinococcosis is a parasitic zoonotic disease, caused by tapeworms of the genus Echinococcus of the family Taeniidae. Epidemiology of echinococcosis involves the domestic cycle as well as the wildlife cycle. The domestic cycle involves the domestic dog and sheep, while the wildlife cycle involves wild carnivores and herbivores. Cystic echinococcosis occurs worldwide except Antarctica. Latest estimates on cystic echinococcosis suggests an annual global incidence of at least 1,88,000 new cases of cystic echinococcosis. The seroprevalence of cystic echinococcosis have shown increasing trends in India. An overall significant increase from 15.0% (1984-2003) to 28.6% seropositivity (2004 – 2015) in humans has been observed in India. India is ranked first in cystic echinococcosis cases with 12% (119,320 cases) reported from India out of 973662 global human cases of cystic echinococcosis. Echinococcosis has great public health and economic impact. Computed tomography, magnetic resonance imaging and ultrasonography are useful for diagnosis of deep-seated lesions in the organs. The disease can be prevented and controlled by continuous surveillance of the disease, regular deworming of animals; slaughterhouse, food and personal hygiene; prevention of dogs to access infected meat and offal; creation of public awareness about the disease; vaccination of animals, especially sheep; combination of disease prevention and control programmes; intersectoral collaboration, and implementation of new surgical techniques for complete resection of cystic echinococcosis and complete resection of alveolar echinococcosis lesions.

Keywords: Alveolar, Cystic, Control, Echinococcosis, Epidemiology, Prevention, Zoonotic

Introduction

Echinococcosis is a parasitic zoonotic disease (naturally transmissible between vertebrate animals and humans), caused by tapeworms of the genus *Echinococcus* of the family Taeniidae. Echinococcosis occurs in four forms. *The cystic,* alveolar, polycystic and unicystic echinococcosis are caused by infection with *Echinococcus granulosus, Echinococcus multilocularis, Echinococcus vogeli and Echinococcus oligarthrus, respectively.* The cystic echinococcosis is also known as hydatid disease or hydatidosis. In humans, the cystic echinococcosis and alveolar echinococcosis are the two most important forms, which are of medical and public health relevance. The most prevalent species are *Echinococcus granulosus* and *Echinococcus multilocularis*, followed by *Echinococcus vogeli* and *Echinococcus oligarthrus* (Siles-Lucas *et al.*, 2017). In humans, hydatidosis occurs worldwide and causes serious public health problems. *Echinococcus granulosus* is more common and *Echinococcus mutilocularis* is the most virulent (Permin and Hansen, 1994). Echinococcosis is a major public health problem in some countries, and it may be emerging or re-emerging in some areas (Moro and Schantz, 2009). Latest estimates on cystic echinococcosis suggests an annual global incidence of at least 1,88,000 new cases of cystic echinococcosis (Rojas *et al*., 2018). *Echinococcus mulitilocularis* is rare but is the most virulent, and *Echinococcus vegeli* and *Echinococcus oligarthrus* are the rarest (Gessese, 2020).

India has a huge livestock population that can act as intermediate hosts to complete the life cycle of the etiological agent. These intermediate hosts graze on pastures contaminated with dog faeces and ingest the echinococcal eggs. High number of stray dog population in both urban and rural areas in India is another risk factor responsible for higher prevalence of *E. granulosus.* Alveolar echinococcosis is non-endemic in India and information about its clinical cases, prevalence and epidemiology is limited (Madhusudhan *et al*., 2016). However, cystic echinococcosis is an endemic zoonosis in many parts of the world including India (Grakh *et al*., 2020).

The seroprevalence of cystic echinococcosis have shown increasing trends in India. An overall significant increase from 15.0% (1984-2003) to 28.6% seropositivity (2004–2015) in humans has been observed in India (Khurana *et al*., 2007; Zaman *et al*., 2017). India is ranked first in cystic echinococcosis cases with 12% (119,320 cases) reported from India out of 973662 global human cases of cystic echinococcosis (Hotez and Damania, 2018). Seroprevalence of cystic echinococcosis in South Kashmir, India was significantly higher among males, children, and illiterate persons (Andrabi *et al*., 2020). Echinococcosis is a parasitic zoonotic disease that has serious health and economic impacts. Therefore, a systematic review on the disease is important to provide the updated information associated with the past and current status of the disease in India as well as the world and recent development in the diagnosis and prevention and control of the disease.

Etiology

Echinococcosis is caused by tapeworms of the genus *Echinococcus,* belongs to the family Taeniidae. *Echinococcus spp.* is a tiny tapeworm, about 2-7 millimeters in length. Echinococcosis is caused mainly by four species of *Echinococcus*, viz., *Echinococcus granulosus, Echinococcus multilocularis*, *Echinococcus vogeli* and *Echinococcus oligarthrus.* These species are morphologically distinct in both the adult and the larval stages. In addition, several different strains of *Echinococcus granulosus* and *Echinococcus multilocularis* are recognized (FAO, 1982). Two new species of *Echinococcus* have recently been identified, *Echinococcus shiquicus* in small mammals from the Tibetan plateau and *Echinococcus felidis* in African lions, but their zoonotic transmission potential is unknown (Moro and Schantz, 2009).

Epidemiology

The lifecycles of *Echinococcus granulosus* can be classified as the domestic cycle and the wildlife cycle. The domestic cycle involves the domestic dog as the principal definitive host and various species of domestic ungulates as intermediate hosts, while, the wildlife cycle involves wild carnivores and ungulates as hosts (Eckert and Deplazes, 2004). Within the cycles, the specific role of various host species may differ considerably between regions of endemic infection. In many endemic areas, the domestic and the sylvatic lifecycles coexist or overlap. Cystic echinococcosis occurs worldwide except Antarctica. A few island countries have declared elimination of cystic echinococcosis (Craig *et al*., 2007). Alveolar echinococcosis is confined to the Northern Hemisphere particularly in the regions of China, the Russian Federation and countries in continental Europe and North America. More than 1 million humans are affected with echinococcosis at any one time. In endemic regions, the incidence rates of human cystic echinococcosis can reach more than 50 per 100 000 person-years. The prevalence levels are 5%–10% in parts of Argentina, Central Asia, China, East Africa and Peru. The prevalence of cystic echinococcosis in livestock from slaughterhouses in hyperendemic areas of South America varies from 20%–95% of slaughtered animals (WHO, 2020).

Cystic echinococcosis is highly endemic in Western China, Central Asia, South America, Mediterranean countries and Eastern Africa, and the main risk factors being contact with dogs and raising livestock (Craig *et al*., 2007; Zhang *et al.* 2015). Five thousand new cystic echinococcosis cases are still diagnosed annually in Argentina, Brazil, Chile, Peru, and Uruguay (Larrieu and Zanini, 2012; Pavletic *et al.*, 2017). Cystic echinococcosis has been declared provisionally free of the disease from New Zealand, and Tasmania in Australia (Craig *et al.*, 2017); nevertheless, *Echinococcus granulosus* is present on the Australian mainland and is still found in Tasmanian dogs, but at low prevalence (Jenkins *et al.*, 2014) in humans, alveolar echinococcosis is a life-threatening disease caused by the larval stage of *Echinococcus multilocularis* (Guo *et al.*, 2021).

Alveolar echinococcosis has been a public health concern in Northern Japan for the past 40 years (Vuitton *et al.*, 2011; Irie *et al*., 2018). High incidence of alveolar echinococcosis has been reported on the Tibetan plateau using mass screening with serology and ultrasound in China (Feng, *et al.*, 2015) and showed the higher prevalence of alveolar echinococcosis in children than that of cystic echinococcosis in several areas (Cai *et al*., 2017). Among the 18,235 estimated new cases of alveolar echinococcosis per year globally, the prevalence is higher (91%) in China (Torgerson *et al.*, 2010). Alveolar echinococcosis is also endemic in Central Asia, with high endemicity of both *Echinococcus multilocularis* and *Echinococcus granulosus* in Kazakhstan and Kyrgyzstan (Abdybekova *et al*., 2015; Counotte, *et al*., 2016).

In Europe, the prevalence of *Echinococcus multilocularis* in definitive and intermediate hosts increased markedly within the first 15 years of this century, and the geographic distribution of infections in fox has been increased than earlier reported; urban foxes may be involved in transmission (Berke *et al*., 2005; Craig *et al*., 2017). *Echinococcus multilocularis* is endemic in North America, Northwestern Alaska, Northwestern Canada and the North-Central United States, but geographic range of the parasite appears to be expanding due to increased and improved sampling efforts and the targeting of definitive hosts other than foxes such as coyotes (Deplazes *et al.*, 2017). Geographically distinct strains of *Echinococcus granulosus* exist with different host affinities. Ten distinct genotypes (G1-10) within *Echinococcus granulosus* have been identified through molecular studies using mitochondrial DNA sequences (McManus and Thompson 2003). These genotypes include G1 and G2 in sheep, G3 and G5 in bovine, G4 in horse, G6 in camel, G7 in pig and G8 in cervid. A G9 genotype has been reported in swine in Poland (McManus and Thompson, 2003) and G10 in reindeer in Eurasia. The genotype G1 is the most cosmopolitan form and most commonly associated with human infections.

In India, the annual incidence of echinococcosis varies from 1 to 200 per 100,000 populations. High prevalence was reported from Kashmir, Andhra Pradesh, Tamil Nadu and Central India (Parikh, 2012). Cystic echinococcosis is endemic in many regions in India, as is evident by hospital-based studies (Fomda *et al.*, 2002), case reports (Biswas *et al*., 2010), and seropositivity to hydatid fluid antigens in asymptomatic subjects (Fomda *et al*., 2015), however, detailed epidemiological studies from India are scanty (Fomda *et al*., 2015). Sero-epidemiological study revealed that out of 1429 asymptomatic persons residing in different districts of Kashmir (North India), 5% were seropositive (Malla *et al*., 2016). Echinococcosis is a neglected parasitic zoonosis in the developing country like India. In Maharashtra state of India, the highest the prevalence of echinococcosis was found in cattle (3.00%) followed by buffalo (2.05%), pig (1.28%), sheep (0.09%) and goat (0.01%), by post-mortem examination (Vaidya *et al*., 2018).

Host Range

Probably *Echinococcus granulosus* originally completed its life cycle among wild animals in a sylvatic cycle that involved wolves and cervids or lions and warthogs. It has now adapted into a domestic cycle, however, commonly involving dogs and sheep (FAO, 1982; Soulsby, 1982). As *Echinococcus granulosus* has little host specificity with regard to intermediate hosts, hydatid cysts have been seen in a wide range of mammals such as domestic ruminants, different types of deer, pigs, equines, camels, giraffes, hippopotamuses, elephants, marsupials and humans (FAO, 1982; Raush, 1986).

Risk Factors

Cystic echinococcosis is most commonly found in people involved in raising sheep, as a result of the sheep's role as an intermediate host of the parasite and the presence of working dogs that are allowed to consume the offal of infected sheep. Alveolar echinococcosis is typically found in older people.

Economic Impact

The prevalence of echinococcosis is highest in rural areas where older animals are slaughtered. Economic losses incur in the form of condemnation of the part (especially liver) of slaughtered animals, carcase weight loss, inferior hide quality, decrease of milk production, and reduced fertility. Economic losses also incur in the form of reduction in the performance and expenses in hospitalization of human cases, diagnosis, and treatment including surgery especially in case of hydatid cysts in vital organs like brain, liver, lungs etc. Both cystic echinococcosis and alveolar echinococcosis are often expensive and sometimes require extensive surgery and/or prolonged treatment. A total annual loss of Rs. 11.47 billion in India is estimated with cattle and buffalo population affected with cystic echinococcosis and this itself is an understatement owing to under reporting of the disease in animals, however, the losses due to surgical interventions, loss of productivity and hospital due to cystic echinococcosis in humans were estimated to be Rs. 472.72 million (Singh *et al*., 2014). Globally, the costs associated with cystic echinococcosis are estimated to be US$ 3 billion annually for treating cases and losses to the livestock industry (WHO, 2020).

Lifecycle

The adult stage of the parasite is found in the small intestine of the definitive host, from where eggs are passed with the faeces. When eggs are ingested by the intermediate host, the eggs are immediately infective, releasing larvae that penetrate into the lymphatic or vascular system, reaching the liver, lungs and other organs. The hydatid cyst develops slowly over several months or even years. The hydatid cyst forms an outer laminated membrane and an inner membrane (the germinal layer). From the germinal layer the brood capsules develop. Each brood capsule contains one or several invaginated heads (protoscolices) that can develop into the adult tapeworm upon ingestion by the definitive host (Soulsby, 1982).

Transmission

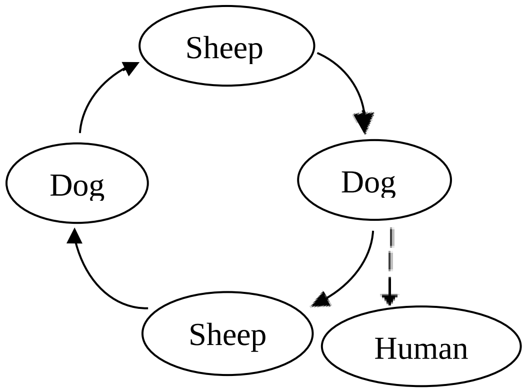

Figure 1: Transmission Cycle of Echinococcosis

Echinococcus spp. is cestode parasite which requires two types of hosts that are intermediate hosts (a large number of herbivorous and omnivorous animals) and definitive hosts (carnivorous animals). The intermediate hosts become infected by ingesting the food and water contaminated with parasite eggs. The parasite develops into larval stages in the viscera of the intermediate hosts. Humans act as so-called accidental intermediate hosts because they acquire infection in the same way as other intermediate hosts, but are not involved in transmission of the infection to the definitive host. Humans become infected by ingesting the food and water contaminated with parasite eggs or after direct contact with animal hosts. The definitive hosts harbour the mature tapeworm in their intestine. The definitive hosts are infected through the consumption of visceral organs of intermediate hosts that contain the larvae of the parasite. Alveolar echinococcosis usually occurs in a wildlife cycle which involves foxes or other carnivores and small mammals like rodents (act as intermediate hosts). Domesticated dogs and cats can also act as definitive hosts.

There are several distinct genotypes of *Echinococcus granulosus.* Some genotypes have distinct intermediate host preferences. All genotypes do not cause infections in humans. The genotype causing the great majority of cystic echinococcosis infections in humans is principally maintained in a dog–sheep–dog cycle. However, several other domestic animals may also be involved, including cattle, goats, swine, camels and yaks. The disease may also be transmitted through inhalation of dust contaminated with infected eggs. Infection may also occur due to handling or playing with infected dogs (hand to mouth transfer of eggs).

Public Health Significance

Echinococcosis is a major helminthic cyclozoonosis of great public health and economic significance (Pal and Dutta, 2013). Echinococcosis may cause inapparent infection to severe and fatal disease in humans. Persons infected with cystic echinococcosis often remain asymptomatic until hydatid cysts containing the larval parasites grow large enough. Cyst rupture most frequently occurs due to trauma and may cause mild to severe anaphylactic reactions, even death, as a result of the release of cystic fluid. The incubation period in cystic echinococcosis in humans varies greatly which may be few years. Human infection with *Echinococcus granulosus* leads to the development of one or more hydatid cysts (cystic echinococcosis or hydatid disease) located mostly in the liver and lungs, and less frequently in the kidneys, spleen, muscles, central nervous system and bones. The disease is characterized by nausea, vomiting and abdominal pain mainly due to involvement of hydatid cysts in the liver. Chronic cough, chest pain and shortness of breath occur due to development of hydatid cysts in the lungs. Other signs may occur depending on the location of the hydatid cysts and the pressure exerted on the surrounding tissues.

The incubation period in alveolar echinococcosis in humans varies from 5 to 15 years. Alveolar echinococcosis in humans is characterized by the slow development of a primary tumour-like lesion (usually located in the liver), abdominal pain, signs of hepatic failure, general malaise and weight loss. Metastases of larvae via the blood and lymphatic system may lead to their spread to spleen, lungs and the brain. Alveolar echinococcosis may be fatal to untreated cases. Approximately 2.2% post-operative death rate for surgical patients occurs in cystic echinococcosis, and about 6.5% of cases relapse after an intervention, thereby requiring prolonged recovery time (WHO, 2020).

Diagnosis

New sensitive and specific diagnostic methods and effective therapeutic approaches against echinococcosis have been developed in the last 10 years (Bhutani and Kajal, 2018). Important diagnostic methods are as follows-

1. Clinical Diagnosis

The presence of a cyst-like mass in a person with a history of exposure to sheep and dogs in an area where *Echinococcus granulosus* is endemic, suggests a diagnosis of cystic echinococcosis.

2. Radiological Diagnosis

Radiography is useful for detection of echinococcal cysts in the lungs; in other sites, however, calcification is necessary for radiographic visualization. Computed tomography, magnetic resonance imaging, and ultrasonography are useful for diagnosis of deep-seated lesions in all organs and also for determination of the extent and condition of the avascular fluid-filled echinococcal cysts. In humans, the ultrasonography imaging is the technique of choice for the diagnosis of both cystic echinococcosis and alveolar echinococcosis. This technique is usually complemented or validated by computed tomography and/or magnetic resonance imaging scans. Abdominal ultrasonography is the most widely used imaging technique for echinococcosis due to its widespread availability and usefulness for determining the number, site, dimensions, and vitality of echinococcal cysts (Pawlowski *et al.*, 2001).

3. Serological Diagnosis

Specific antibodies can be detected by different serological tests, which can be supportive in the diagnosis. ELISA is preferred method, but complement fixation, indirect agglutination and latex agglutination tests can also be used. Early detection of *Echinococcus granulosus* and *Echinococcus multilocularis* infections, especially in low-resource settings is still useful in the selection of clinical treatment options. Hydatid fluid is the major antigenic source for echinococcosis immuno-diagnosis, with the hydatid fluid lipoproteins antigen B (AgB) and antigen 5 widely used in serological assays for cystic echinococcosis (McManus *et al.*, 2012). Serology is not useful as a first-intent diagnostic tool for mass screening in endemic areas, where a proportion of the human population exhibits positive serology without alveolar echinococcosis lesions (Bartholomot *et al*., 2002).

4. Intradermal Test (Casoni Test)

A skin test is carried out with antigen derived from hydatid fluid. This test is still in wide use.

Prevention and Control

Despite some progress in the control of echinococcosis, the disease continues to be a major public health problem in several countries, and in several others it constitutes an emerging and re-emerging disease (Moro and Schantz, 2009). The following strategies are useful for prevention and control of echinococcosis.

1. Surveillance

Surveillance of the disease is important to assess the economic burden due to the disease and to evaluate the progress and success of the disease control programmes. However, surveillance for cystic echinococcosis in livestock and dogs is difficult due to asymptomatic infection in them. Moreover, surveillance is not recognized or prioritized by communities or local veterinary services.

2. Deworming of Animals

Cystic echinococcosis is a preventable disease as it involves domestic animals (definitive and intermediate hosts). The disease prevention programmes should focus on periodic deworming of dogs with praziquantel, at least 4 times annually. Prevention and control of alveolar echinococcosis is more complex as the transmission cycle involves wild animals (definitive and intermediate hosts). Regular deworming of domestic carnivores that have access to wild rodents can reduce the risk of human infection. Deworming of wild and stray definitive hosts with praziquantel baits have been found effective in reducing the prevalence of alveolar echinococcosis.

3. Slaughterhouse Hygiene

It is important to adopt improved hygienic practices in the slaughtering of livestock. Moreover, the viscera containing hydatid cysts from slaughtered animals must be properly destroyed or disposed of to avoid direct access by dogs (definitive host).

4. Food and Personal Hygiene

Proper food hygiene and personal hygiene especially, those having close contact with pets are important in prevention and control of the disease. Children playing with pet dogs should wash their hands to avoid faeco-oral transmission of the disease. Measures should also be adopted to prevent the contamination of food and water with dog faeces.

5. Breaking the Lifecycle of the Etiological Agent

Echinococcosis can be controlled through preventive measures that break the cycle between the intermediate host and the definitive. These preventive measures include inspecting meat, dosing dogs, and educating the public on the risk to humans and on avoiding feeding infected offal to dogs, and introducing legislation.

6. Public Education

Creation of public awareness about the public health significance, transmission, prevention and control of the disease is important in prevention and control of echinococcosis. Public education campaigns particularly for dog owners, butchers, animal breeders and shepherds have been found effective in lowering the disease incidence, preventing the disease transmission and alleviating the burden of the disease in human.

7. Vaccination

Vaccination of sheep with an *E. granulosus* recombinant antigen (EG95) is important in prevention of the disease in sheep (intermediate host) and hence in humans. This vaccine has been promoted as a complementary intervention to eliminate cystic echinococcosis transmission (Larrieu and Zanini, 2012).

8. Treatment

The treatment varies from minimally invasive treatments (percutaneous drainage) or medical therapies to surgical intervention. Percutaneous drainage of the cyst is a good option in selected cases (Bhutani and Kajal, 2018). There are four options for the treatment of cystic echinococcosis in humans, which includes percutaneous treatment of the hydatid cysts with the PAIR (Puncture, Aspiration, Injection, Re-aspiration) technique, surgery, anti-infective drug treatment with albendazole and watch and wait. *Echinococcus granulosus* cysts can be removed surgically, but there is risk of accidental spillage of viable scolices into the body cavities may cause anaphylactic reaction, and moreover, is likely to lead to development of fresh cysts. Therefore, hydatid cyst is first injected with a scolicidal agent such as chlorhexidine or hydrogen peroxide to prevent the problems associated with viable scolices.

9. Combination of Programmes

A combination of programmes of vaccination of lambs, deworming of dogs and culling of older sheep have been found effective in eliminating the cystic echinococcosis in humans in less than 10 years (WHO, 2020).

10. Intersectoral Collaboration

Collaboration between veterinarians and public health workers is important in the prevention and control of the disease.

Conclusion

Echinococcosis is a parasitic zoonotic disease, causing serious animal and public health problems and economic impact. The etiological agent of echinococcosis has a wide host range including domestic and wild animals, and humans. Moreover, the epidemiology of *Echinococcus* spp. is complex due involvement of wild animals in its lifecycle. Therefore, there is need of reliable technologies for accurate diagnosis of the disease. Continuous epidemiologic surveillance of the echinococcosis in dogs and wild animals like foxes, wolves etc.; regular deworming of animals; slaughterhouse, food and personal hygiene; prevention of dogs to access infected meat and offal; creation of public awareness about public health significance and other aspects of the disease; vaccination of animals, especially sheep; combination of the disease prevention and control programmes; collaboration between veterinarians and public health workers; and new surgical techniques for complete resection of cystic echinococcosis and complete resection of alveolar echinococcosis lesions are important for prevention and control of echinococcosis in animals and humans as well as improving the quality of life of patients.

Conflict of Interests

There is no conflict of interest.

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