International Journal of Livestock Research, Vol. 10 (7) July' 2020
http://www.ijlr.org
eISSN: 2277-1964
NAAS Rating 2020 – 5.36

Review Article

Epidemiology, Risk Factors and Economics of Echinococcosis in India: A Review

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How to cite this paper: Grakh, K., Prakash, A., Mittal, D., Kumar, P., & Kumar, R. (2020). Epidemiology, Risk Factors and Economics of Echinococcosis in India: A Review. *International Journal of Livestock Research*, 10(7), 1-10. doi: http://dx.doi.org/10.5455/ijlr.20200418070900

Received : Apr 18, 2020
Accepted : Jun 06, 2020
Published : Jul 31, 2020

Abstract

Echinococcosis caused by cestode of genus Echinococcus is an important zoonotic disease with worldwide distribution. Two of the important echinococcosis are cystic echinococcosis (CE) and alveolar echinococcosis (AE) caused by metacestodes of Echinococcus granulosus and E. multilocularis, respectively. The definitive hosts for CE or hydatidosis are carnivores and intermediate hosts are herbivores, with humans acquiring the accidental infection from carnivores. The larval stages of E. granulosus can parasitizes internal organs of animals and humans and as a result responsible for substantial morbidity and mortality. Worldwide, India is ranked first in CE cases amounting to 12% of global CE cases. Apart from morbidity and mortality in humans and animals, the economic losses in animals arise from production losses, condemnation of cyst affected carcasses, and losses from poor reproductive performances. The data regarding the losses in animals is often underreported. In humans, 8,71,000 disability- adjusted-life- years (DALY) globally each year points toward the severity of the disease. The various risk factors such as illegal slaughter/ slaughter in uncertified slaughterhouses, large population of stray dogs, dependency of rural population to raise livestock and practice of feeding dogs with offal of home butchered animals facilitate CE transmission in India, which makes it a public health, veterinary and social challenge. Systematic and national level surveillance of disease in rural livestock and human population, awareness programmes about its zoonotic nature, coordinated efforts from veterinary and medical science for epidemiology and diagnosis, and strict legislation in post mortem inspection at abattoirs is needed for prevention and control of the disease.

Keywords: Abattoir, Echinococcosis, Host, Zoonosis

Introduction

Echinococcosis is a neglected zoonotic parasitic infection caused by the larval stage of tapeworm parasite belonging to the genus *Echinococcus*. The life cycle of this tapeworm is sustained between dogs (definitive host) and herbivores (intermediate host). Humans can also develop the disease owing to consumption of food stuff contaminated with dog faeces. *Echinococcus granulosus* causes cystic echinococcosis (CE) whereas *Echinococcus multilocularis* is responsible for alveolar echinococcosis (AE). AE is non-endemic in India and information about its clinical cases, prevalence and epidemiology is limited (Madhusudhan *et al*., 2016). However, CE is an endemic zoonosis in many parts of the world including India. The larval stages of *E. granulosus* can parasitizes liver, lung, lung and other organs of humans, cattle, buffalo, sheep, pigs and other animals (Haridy *et al*., 2006). It is recognized as one of the seventeen neglected human diseases in the world with more than one million human cases (WHO, 2018). India is ranked first in CE cases with 12% (119,320 cases) reported from India out of 973662 global human CE cases (Hotez and Damania, 2018). Because of the involvement of canines, herbivores and human, the CE is the disease of high public health, veterinary and socioeconomic importance in India as well as the world.

Echinococcosis persists mainly in domestic cycle involving domestic dog as definitive host and various species of domestic animals as intermediate hosts. The *E. granulosus* eggs can survive under warm, humid and cold climatic conditions for weeks to months, but sensitive to desiccation (Eckert *et al*., 2003). CE is distributed worldwide in human and animal population with highest prevalence found in parts of Eurasia, Africa, Antarctica and South America (Eckert and Deplazes, 2004). However, Iceland and Greenland islands are free from *E. granulosus* and only sporadic cases were detected from others such as New Zealand, Tasmania and Southern Cyprus (Eckert and Deplazes, 2004). Echinococcosis or hydatid cysts have been found in cattle, buffalo, sheep and other food producing animals in India. A total annual loss of Rs. 11.47 billion in India is estimated with cattle and buffalo population affected with CE and this itself is an understatement owing to under reporting of the disease in animals (Singh *et al*., 2014a). However, the losses due to surgical interventions, loss of productivity and hospital due to CE in humans were estimated to be Rs. 472.72 million (Singh *et al*., 2014a). Unplanned or illegal slaughtering, large population of stray dogs, improper disposal of dead animals and close association of rural population with animals increase the possibility of disease transmission to humans. Latest estimates on CE suggests annual global incidence of at least 1,88,000 new CE cases (Rojas *et al*., 2018). Around 12% of the global CE cases are from India which is because of favorable climatic conditions such as warm and humid climate, availability of large numbers of intermediate host dependent on grazing activities, lack of awareness and poor collaboration between veterinary and medical sciences in India. The present article emphasizes the epidemiological aspects, risk factors and economic losses associated with the disease.

Life Cycle

The life cycle of these parasites is indirect and requires two mammalian hosts i.e. definitive and intermediate hosts. The life cycle starts with the adult stage of the parasite in small intestine of the dogs or other canids (definitive host). The definitive host pass the parasitic eggs in faeces which contaminate the soil, pasture, vegetable gardens and water sources like ponds in the environment. In the environment the eggs can remain viable for weeks to months up to a wide temperature range of 38°C to -30°C, however infectivity tends to decrease as the temperature increases (NCDC, 2016). After ingestion of contaminated food stuff by intermediate hosts (domestic or wild ungulates), eggs hatches in small intestine and release larval stage (oncosphere) that penetrates the intestinal wall. Through intestinal blood vessels, the oncosphere reaches various organs, especially liver and lungs. In these organs, the oncosphere develops into second stage known as metacestode which are cystic structure, typically filled with clear fluid (hydatid fluid) that enlarge to produce protoscolices and daughter cysts. These cysts infesting various visceral organs of the intermediate host are ingested by the definitive host. In the small intestine of definitive host protoscolices evaginate, attach to intestinal mucosa and develop into adult stages in 32 to 80 days thereby completing the life cycle (Thompson and Lymbery, 1990). Humans acquire the infection through accidental ingestion of the eggs, which in turn develop into the parasite’s larval stage (metacestode) in internal organs and ultimately CE. The exact time required for development of various stages of cyst in humans is not known, but it is estimated to be more than 10 months post infection (Eckert and Deplazes, 2004). Human act as dead-end host in the disease transmission cycle.

Clinical Signs

The disease is primarily asymptomatic in definitive and intermediate animal hosts. In humans, the disease may remain asymptomatic for years, and signs and symptoms may appear subject to the organ affected and severity of infection (WHO, 2018). However, irrespective of the location of cyst, the primary symptoms in affected human population include pain in abdomen, followed by lump in abdomen (Rao *et al.*, 2012). In addition, the symptoms may vary depending upon the localization of the cyst (Sharma *et al*., 2013).

Predisposing Factors

Sex/Gender

The conflicting reports exists indicating sex as a predisposing factor for the disease in humans and animals. Higher rate of infection in females have been observed in goats and it is possible because of longer survival period of parasite in females due to potential link between sexual hormones and response of the immune system (Blancas *et al*., 2007; Godara *et al*., 2014). Other possible reason might be that female animals are slaughtered at older age as they are retained for reproductive purposes and therefore longer life expectancy provides more chances of exposure to the infection (Ibrahim, 2010). Similarly, in humans higher cases are observed in females as compared to males (Rao *et al*., 2012). The reasons might be due to the fact that in rural communities, females are more involved in livestock management activities and hence have more chance to acquire the disease from environmental contamination (Singh *et al*., 2014a). On contrary, some hospital-based seroprevalence studies in humans and abattoir-based studies in animals have not found any significant differences in gender predisposition (Khurana *et al*., 2007; Zaman *et al*., 2017; Ganaie *et al*., 2018). So, no consensus can be found or established regarding predisposition of sex in the disease.

Age Group

Incidence of CE is higher in older animals as compared to younger ones and this finding is consistent with animal population viz. cattle, sheep, goat, pig, buffaloes (Singh *et al*., 2012; Otero-Abad and Torgerson, 2013). A study carried out in sheep and goats recorded 1.6 times higher hydatidosis prevalence in older sheep and goat (more than three years old) as compared to young ones (Marshet *et al*., 2011). It could be because most female sheep and goats, which are retained for reproductive purposes, are sent for slaughter at old age and therefore diagnosed at older age as compared to young ones. In humans, most commonly affected age group ranges from 17-50 years (Rao *et al*., 2012; Gochhait *et al*., 2015). It may be due to the fact that as infection remain asymptomatic in animals and humans and also parasite has a long incubation period, hence, most of the cases are diagnosed at an older age (Craig *et al*., 2017).

Seasonal Pattern

Seasonal influence has been the least studied parameter and does not seem to have any significant effect on the disease prevalence among intermediate hosts (Ganaie *et al*., 2018).

Organ Predilection

Irrespective of the species of intermediate animal host, liver and lungs are observed as most commonly affected or predilected area for hydatid cyst formation. Liver as well as lungs are considered as most affected organs in animals (Pednekar *et al.* 2009; Singh *et al*., 2012; Godara *et al*., 2014; Sajjan *et al*., 2015). Other organs involved are spleen, heart, kidney, mesentery and diaphragm. In humans, liver is found to be most affected organ followed by lungs. Rare cases of skeletal cysts are also found in humans (Rao *et al*., 2012; Sharma *et al*., 2013).

Risk Factors for the Disease

The suitable conditions for the establishment and transmission of Echinococcosis exist in India such as large population of intermediate hosts, close contact of human-dog and dog and intermediate host, browsing and grazing on contaminated pasture, warm and humid and cold climate conditions during different part of seasons (Singh *et al.*, 2014a). India has a huge livestock population of 536.76 million, out of which 536.16 million can act as intermediate hosts to complete the life cycle (20^{th} Livestock Census, 2019). 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* (Table

1). These stray dogs receive no or an inadequate treatment with anti-parasitic medications and thus they play an important role in the transmission of the disease in the country. Open dumping of dead animals in rural part of the country with an easy access to stray dogs further complicate the problem. Pet dogs as guarding animals, dog owners, animal handlers, veterinarians and laboratory workers are also at higher risk of infection, since the eggs can contaminate water, fruits and vegetables. These eggs can stick to the fur of an animal and get transferred from hands to the mouth of humans in absence of personnel hygiene. Shephard dogs have been found to be at higher infection risk as compared to stray dogs, due to their free access to offals and other animal wastes (Otero-Abad and Torgerson, 2013). Frequent contact of rural human population with animals due to their dependency on livestock for income, transportation, cultivation etc. is another risk factor. Other factors like lack of awareness about the parasite, inappropriate meat inspection at slaughterhouses and offal disposal by illegally run abattoirs also contributes to domestic cycle of transmission.

Table 1: Prevalence (%) of *E. granulosus* in stray dog population in India

Location/State	Prevalence	Reference
Kurnool, Andhra Pradesh	33.3	Reddy *et al*., 1958
Delhi and Uttar Pradesh	14	Singh and Dhar, 1988
Assam	17.02	Deka *et al*., 2008
Mizoram	18.18	Deka *et al*., 2008
Meghalaya	27.77	Deka *et al*., 2008
Bangalore urban, Karnataka	4.35	Prathiush *et al*., 2008
Maharashtra	5.22 - 6.57	Nikale *et al*., 2014; Ingole *et al*., 2018
Gurugram, Haryana	13.5	Varma, 1990

Prevalence of *E. granulosus*

Accurate diagnosis and prevalence of *Echinococcus* infection in the intermediate and definitive hosts is an important component for establishing echinococcosis and preventing human and livestock infection (Moon and Khemalpure, 2017). The already published data related to echinococcosis in dog (Table 1) and livestock population (Table 2) indicates significant prevalence of disease in parts of India. As per 20th livestock census, 2019, the total dog population is 9.43 million in India. But according to other animal welfare groups and websites the country is home to about 30 million stray dogs, which amounts to 1 stray dog per 42 people in the country (Socialcops, 2020; Statista, 2020). From the various published reports, (Table 1) the range of *E. granulosus* infection in stray dog population vary from 4.35% in Karnataka to 33.3% in Andhra Pradesh in India.

The available data indicate that cattle, buffalo, sheep, goat and pig play an important role as intermediate hosts in India. The higher prevalence in all the intermediate hosts might be due to the grazing of these animals on contaminated pastures or by drinking dog feces contaminated water (Otero-Abad and Torgerson, 2013). Since CE is asymptomatic in animals, abattoir-based studies relied for prevalence data in domestic livestock animals. Most of these studies took place in large abattoirs where animals are brought from random places that are intensively managed or large-scale production system. The studies involving urban based abattoirs, hence may indicate irrelevant diseases prevalence in rural communities, which is expected to be significantly higher (Pednaker *et al*., 2009). Most of studies reportedly claiming prevalence of CE in specific region of India (north, south, east and west) are based upon the abattoir data in that particular location or region, hence such studies may not actually reflect true prevalence and actual prevalence is expected to be higher.

The seroprevalence against CE 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). WHO has recommended the use of clinical and laboratory data of hospital cases as practicable indicator of the incidence of the disease in humans.

Table 2: Zone and state wise prevalence (%) of CE in intermediate hosts

Region	Prevalence					Literature
	Cattle	Buffalo	Sheep	Goat	Pig	
Northern India						
Haryana			4.7	1.9	1.3	Varma, 1990
Punjab	7.6	8.9-50.96	5.1	2.8	4.66	Deka *et al.*, 1983, Sharma *et al* 2004, Jadhav *et al*., 2013, Khan *et al.*, 2013
HP			7.2	2.3		Jitendran, 1996
J&K				19.8		Godara *et al*., 2014
Uttar Pradesh		14.82- 36	2.56-6	1.45-2	0.9-1.42	Deka and Gaur 1998, Varma and Malviya 1992, Irshadullah *et al*., 1989; Ganaie *et al*., 2018
Delhi			18.5			Rana *et al*., 1986
Diff. Location	5.39	4.36	2.23	0.41	3.09	Singh *et al*., 2014b
Diff. Location		48.1	30.50%	21		Singh and Dhar, 1988
Range	5.4-7.6	4-51	2.2-30	0.41-21	0.9-4.6	
Western India						
Maharastra	5.1	3.81	0.02-1.06	0.3	0.87	Pednekar *et al*., 2009, Gatne 2001
Rajashthan			6.57	4.12		Shekhawat *et al*., 2005
MP		1.19				Jatav and Garg, 2012
Range	5.1	1.2-3.8	0.02-6.6	0.3-4.1	0.9	
Southern India						
AP			5.18-7.05	1.39		Pillai *et al.*, 1986; Hafeez *et al.*, 1994
Chennai			5.6-22.4	7-25.8		Sangaran *et al*., 2014; Shanmugam *et al.*, 1994
Karnataka			0.37-4.9	4.78		Vijayasmitha *et al*., 1993
Kerala	35.47	33	2.55	1.05		Abraham *et al*., 1980
Diff. Location	7.1	9.4	7		11.5	Hafeez,1997
Range	7.1-35.4	9.4-33	0.4-22.4	1.0-25.8	11.5	
Eastern India						
Assam	16	6.52		2.24-4.9	0.43-1.8	Sarma *et al*., 2000; Deka *et al*., 2008
Bihar				8.48	7.6-8.25	Kumar *et al.*, 2007; Prasad, 1981
Meghalaya	21.40%				0.34	Deka *et al*., 2008
Pudduchery			47.6	37.8		Das and Sreekrishnan, 1998
Sikkim			50	33.3		Katiyar and Sinha, 1981
West Bengal			10.5	3.9	8	Biswas *et al*., 1989; Das and Das, 1998
Range	16-21.4	6.5	10.5-50.0	2.2-57.8	0.3-8.3	
Overall	1.6-35.4	1.2-51	0.02-50	1.05-57.8	0.3-11.5	

Molecular epidemiology of *Echinococcus* species

Mitochondrial DNA sequences have identified 10 different genetic types of *E. granulosus* from G1 to G10 (Craig *et al.,* 2007). Livestock from eastern India demonstrated the presence of four genotypes G1 (sheep strain), G2 (Tasmanian sheep strain), G3 (buffalo strain) and G5 (cattle strain) (Bhattacharya *et al.*, 2007). In northern India, 77.7% of isolates from cattle, pig, buffalo and goat were grouped under G3 strain and 22.2% isolates from sheep are grouped under G1 strain (Singh *et al*., 2012). Four different genotypes i.e. G1, G2, G3 and G5 are demonstrated in food producing animals viz. cattle, buffalo, sheep and pigs in western India (Pednekar *et al.*,2009). G5 (*E.*

ortleppi) is only reported in India (Pednekar *et al*., 2009). The abattoir-based studies in animals indicate that G3 is most common strain of *E. granulosus* circulating in livestock in India followed by G5, G1 and G2 strain.

The strains of *Echinococcus* spp. circulating in livestock in India are well adapted to cause infection in all the intermediate hosts of *E. granulosus* including humans, thus proving to be of zoonotic importance. Globally, most of the human cases of CE are found to be infected with G1 strain of *E. granulosus* (Moro and Schantz, 2009). Despite the isolation of G5 and G6 in humans, G1 and G3 remained commonly encountered strains in human CE in India (Sharma *et al.,* 2013). The wide variation in *E. granulosus* strains may influence the life-cycle patterns, development rate, specificity to host, transmission, antigenic proteins in fluid and response to treatment (Craig *et al.,* 2007).

Diagnosis

In the intermediate hosts, diagnosis of the disease depends on the meat inspection or post-mortem detection of the larval cyst form which can occur in almost any organ particularly in the liver and lungs (Siles-Lucas *et al*., 2017). In live animals, ultrasonography and radiography have been used previously to detect the presence of cysts in lungs and abdominal cavity. However, demonstration of scolices, hooklets or protoscolices in aspirated fluid (fine needle aspiration/ultrasound guided aspiration) by direct microscopic examination or stained smears is definitive diagnosis of cystic echinococcosis (Singh *et al*., 2014a). Molecular methods especially PCR are used widely to characterize *Echinococcus* spp. nowadays and proved to be of great value in identification of *Echinococcus spp.* in samples collected from livestock at abattoirs for epidemiological purposes (Cardona and Carmena, 2013). Serological tests using ELISA are not much reliable in diagnosis of echinococcosis in intermediate hosts (Siles-Lucas *et al*., 2017). The diagnosis of echinococcosis in definitive hosts (dogs or other carnivores) requires the demonstration of the adult cestodes of *Echinococcus* spp. in their faeces or small intestine or detection of specific coproantigens (using ELISA) or copro DNA (using specific primer-based PCR amplification). Sedimentation and counting technique (SCT) for eggs in feces of canines are regarded as the 'gold standard' for assessing the sensitivity and specificity of other techniques (Eckert *et al*., 2003). However, the copro-DNA (PCR) test has a greater sensitivity than SCT.

In humans, non-invasive imaging techniques such as CT scans, MRI and ultrasonography (USG) are used for detecting and defining the extent and condition of avascular fluid-filled cysts in most organs. CT and USG are widely used for screening, clinical diagnosis, and monitoring of treatment of lungs and liver and intra-abdominal cysts respectively (Giri and Parija, 2012). Radiography can also be used in the cases where cyst calcification is suspected. MRI is very useful tool for diagnosis of rare cerebral hydatid cysts and helpful in diagnosing multiple cysts and cyst capsules (Bukte *et al*., 2004). However, serological tests (ELISA and indirect hemagglutination test), are highly sensitive, but specific confirmation can be obtained by detecting echinococcal antigens by immunodiffusion (arc 5) or immunoblot assays (8-, 21 –kD bands) (Eckert *et al*., 2003). Counter current immune-electrophoresis (CIEP) and Casoni's test have been previously used as diagnostic test for hydatid cyst, but not common nowadays (Giri and Parija, 2012). The urine samples are also used for antigen detection as an alternative or in addition to serum because of the non-invasive nature of sample collection and comparable sensitivity and specificity (Sunita *et al*., 2011). Co-agglutination tests has also been found cheap and rapid using urine and serum samples for detection of hydatid antigen (Parija and Shivaprakash, 2000).

Economics of Echinococcosis

Total livestock population of India is 536.76 million (20^{th} Livestock Census-2019). All species except yak, mule, donkey, horse and ponies in India act as intermediate host for echinococcosis. Diseases or infections act as negative input to the production of animal which affect the efficiency of livestock and thus adds to losses (Thrusfield, 2007). The economic losses associated with hydatid disease can be in the form of poor growth, loss of benefits due to condemnation of cyst affected offal mainly liver, production losses by decrease in weight, milk production, wool and fleece/hide value, and reproductive performance (Vaidya *et al.,* 2014). Cost incurred in diagnosis, hospitalization, treatments including surgery, income loss, temporary or permanent disability or impairment and post-operative fatalities in humans which reduces the quality life, throw the light on public health and economic significance of CE. Echinococcosis is estimated to be the cause of 19,300 deaths and around 8,71,000 disability-adjusted life-years (DALYs) globally each year (WHO, 2018). The attempts in food producing animals have been made to calculate the economic cost due to organ condemnation. In Maharashtra, echinococcosis lead to economic losses to the tune of Rs 26, 78, 721 per year (Vaidya *et al*. 2014) due to offal and carcass condemnation. The economic loss due to the condemnation of edible offal in pigs can be as high as Rs. 11,396.10 in some states (Sajjan *et al*. 2015). The systematic analysis of economic losses based on available literature in livestock and humans in India estimated median economic losses to the amount of Rs. 11.47 billion (approx. US $ 212.35 million) where cattle and buffalo industry shared most of the losses i.e. 93.05% of total livestock and 88.88% of the livestock and human losses. Human echinococcosis associated losses are estimated to be Rs. 472.72 million which are likely to be under-estimated due to under-reporting of the disease in the country (Singh *et al*., 2014a).

Conclusion

It can be concluded that CE has significant economic and public health impact worldwide. India have highest number of CE cases (12% of global cases) worldwide. This figure is likely to go up as the disease is often underreported in India. However, the advent of technology, developing health infrastructure, and improved research facilities in the country have facilitated CE diagnosis. In order to aid disease control and prevention, the active surveillance of the disease in livestock and human is needed. The extension programmes about basic hygiene and zoonotic nature of the disease, legalization of slaughter house and proper meat inspection, and combined efforts from medical and veterinary sciences are must to control and prevent disease- associated morbidity and mortality

Conflict of Interests

There is no conflict of interest.

Publisher Disclaimer

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