



Cystic echinococcosis in Jordan: A review of causative species, previous studies, serological and radiological diagnosis

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ABSTRACT

Cystic echinococcosis (CE)/hydatidosis is a zoonotic disease which occur in human and herbivore animals as a result of infection with the larval stage of the taeniid cestode *Echinococcus granulosus* sensu lato (s. l.). In human, CE is a serious public health concern in many parts of the world including Jordan. The present review will cover CE causative agent: *E. granulosus* species/genotypes; life cycle of *E. granulosus* parasite, all published previous studies on CE in Jordan (humans, intermediate hosts, definitive host) as well as its diagnostic methods in human.

1. General introduction

Echinococcosis (synonymous to hydatid disease) is a worldwide zoonosis of human and other herbivore animals, which occurs as a result of infection by the larval stages of the taeniid cestodes of the genus *Echinococcus*. Three forms of echinococcosis are observed in human; cystic echinococcosis (CE) caused by *E. granulosus*, alveolar echinococcosis (AE) caused by *Echinococcus multilocularis*, and polycystic echinococcosis (PE) caused by *Echinococcus vogeli* and *Echinococcus oligarthra* (Nakao et al., 2013; Higueta et al., 2016). The two medically important forms of echinococcosis to human are the CE and AE, where both are considered as serious life-threatening chronic diseases with high fatality rates (Eckert and Deplazes, 2004). The third form, PE, usually results in rare mild diseases and only reported in patients in Central and South America (D'Alessandro and Rausch, 2008; Santos et al., 2012).

Cystic echinococcosis (CE) is global and wider in its distribution than AE and PE especially within communities who raise animals for meat production (Zhang and McManus, 2006). CE affects over 1 million people worldwide and is responsible for the loss of over \$3 billion in terms of medical expenses every year (Higueta et al., 2016). CE was recognized by the World Health Organization as one of the 17 neglected tropical diseases in the world (NTDs) and is also responsible for significant economic losses each year (Torgerson and Macpherson, 2011;

Higueta et al., 2016).

In most Mediterranean basin including Jordan, CE is regarded as an endemic popular disease which has been frequently reported (Sadijadi, 2006; Zhang and McManus, 2006; Hotez et al., 2012; Al-Jawabreh et al., 2017). According to several previous studies on CE in human and animals in Jordan, the disease was observed to be endemic in many areas of the country mainly in the southern cities (Al-Qaoud et al., 2003a). The study by Al-Qaoud et al. (2003a) and the most recent study by Al-Radaideh et al. (2017) reinforced previous findings by Kamhawi (1995), which claimed that CE continues to be of stable endemicity in Jordan as reflected by the consistent surgical incidence in the country since 1985. CE that is caused by *E. granulosus* species will be covered extensively in this review as it is the only reported form in Jordan (Table 1). The present review will shed light on topics related to CE causative agent: *E. granulosus* species/genotypes; life cycle of *E. granulosus* parasite and disease manifestation, previous studies on CE in Jordan (humans, intermediate hosts, definitive host) as well as its diagnostic methods in human.

2. Cystic echinococcosis (CE)

2.1. Causative agent: *E. granulosus* species/genotypes

The causative agent of CE is *E. granulosus* sensu lato (s.l.), which is

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Table 1
Retrospective and seroprevalence studies on CE in human in Jordan.

Study/Reference	Period/years	# of cases involved
Retrospective studies		
Al-Radaideh et al., 2017	2005–2015	217
Alaydi, 2012	2012	27
Daradkeh et al., 2007	1973–1999	169
Yaghan et al., 2004b	1994–2003	65
Al-Qaoud et al., 2003a	1994–2000	472
Dowling et al., 2000	1990–1996	44
Kamhawi, 1995	1985–1993	676
Amr et al., 1994	1976–1986	306
El-Muhtaseb and Shihabi, 1986	1973–1983	132
Shennak et al., 1985	1979–1982	63
El-Muhtaseb, 1984	1973–1982	75
Dajani and Shihabi, 1979	1974–1977	50
Dajani, 1978	1978	26
Sliman, 1976	1967–1969	12
Khoury and Kamhawy, 1966	1966	4
Seroprevalence studies		
Abo-Shehada, 1993	1993	176
Moosa and Abdel-Hafez, 1994	1994	2182
Qaqish et al., 2003	2003	2388

regarded as the most prevalent complex species in the genus *Echinococcus* with a worldwide distribution (Yanagida et al., 2017). *E. granulosus sensu lato* (s.l) was divided into nine formally recognized strains/mitochondrial DNA (mtDNA) lineages, which have been referred to as genotypes (G1–G8 and G10): *E. granulosus* s.s. (G1- cosmopolitan sheep strain, G2- Tasmanian sheep strain, and G3- buffalo strain), *E. equinus* (G4- sporadic horse strain), *E. ortleppi* (G5- sporadic cattle strain), *E. canadensis* (G6- sporadic camel strain, G7- sporadic pig strain, G8- northern arctic cervid strain, G10- Fenno scandinavian cervid strain) and *Echinococcus felidis* (lion strain) (Bowles et al., 1992; Bowles and McManus, 1993a; Bowles and McManus, 1993b; Bowles et al., 1994; Scott et al., 1997; Lavikainen et al., 2003; McManus and Thompson, 2003; McManus, 2013; Nakao et al., 2013; Rojas et al., 2014; Romig et al., 2015). Moreover, recent molecular studies have revealed that *E. granulosus* (s.l) consists of five independent species: *E. granulosus sensu stricto* (s.s.); *E. equinus*; *E. ortleppi*; *E. canadensis* and *E. felidis* (Ito, 2017).

Currently, several valid *Echinococcus* species are known to cause CE in human and various herbivorous animals. These include *E. granulosus sensu stricto* (s.s.), *E. canadensis*, *E. equinus*, and *E. ortleppi* (Nakao et al., 2007; McManus, 2013; Romig et al., 2015; Ito, 2017). However, the majority (88.44%) of human CE cases worldwide are caused the *E. granulosus sensu stricto* G1 genotype (the dog sheep strain), while *E. canadensis* (G6) *E. canadensis* (G7) are responsible for 7.34% and 3.73% of human infections, respectively (Rojas et al., 2014). Furthermore, recent molecular studies observed that many more CE human cases are caused by *E. canadensis* G6/7 and the involvement of other species *E. ortleppi* has also been reported in Africa (Ito et al., 2017; Yanagida et al., 2017).

Several previous studies indicated that the cosmopolitan common sheep/dog strain (G1 genotype) is the dominant strain in Jordan (Al-Qaoud et al., 2003b; Yanagida et al., 2012). However, other *E. granulosus* strains were reported in Jordan including the G4 (horse strain) in donkeys using secondary *in vitro* culture (Hijawi et al., 1992) and *in vivo* development in mice (Al-Abbasi and Abdel-Hafez, unpublished data) as well as RAPD-PCR and RFLP-PCR techniques (Al-Qaoud et al., 2003a), and the camel strain using morphological criteria of metacestode protoscolices (PSCs) (Said et al., 1988). Furthermore, a new study using semi-nested PCR system and mitochondrial *COX1* partial gene sequencing for 139 hydatid cyst isolates from different herbivore host (sheep, goat, cattle and camel) confirmed the dominance of *E. granulosus* s.s. (G1–G3 strains) in Jordan (Issa et al., submitted). No genotyping studies were conducted on hydatid cysts isolated from human

patients, which might reveal that several species/genotypes of *E. granulosus* (*E. granulosus* s.s. (G1–G3 strains) and *E. canadensis* (G6/7)) might be involved in human infections in this country.

2.2. Life cycle and disease manifestation

Cystic echinococcosis (CE), is a chronic parasitic zoonosis which is regarded as a severe and even fatal disease if left untreated. CE is characterized by a long-term growth of the larval stage of *E. granulosus* parasite (known as the metacestode stage) in various organs of human and herbivore animals. The metacestode stage is manifested as fluid-filled hydatid cysts in internal organs, mainly in the liver and lungs. However, hydatid cysts are less frequently seen in spleen, kidneys, heart, bone and central nervous system (Sabouni et al., 2010; Gattu and Bhasha, 2017). While human is regarded as an accidental intermediate host for *E. granulosus*, other herbivore animals such as sheep, cattle, goats and camels are frequently reported to be infected with the larval stage of the parasite. The adult cestode tapeworm of *E. granulosus* inhabits the small intestine of dogs, the definitive host for the parasite who acquires the infection upon eating offals containing mature metacestode stage (hydatid cysts), which contain numerous protoscolices, where each one has the potential to develop into an adult worm in the dog intestine. Upon the maturation of the adult worms, infective eggs start to be released with the infected dog's feces and contaminate the environment. Human as well as other herbivore animals acquire CE upon eating vegetations or drinking water contaminated with the infective eggs (Eckert and Deplazes, 2004; D'Alessandro and Rausch, 2008; Moro and Schantz, 2009).

The hydatid cyst is a fluid-filled, spherical sac consisting of three layers: an inner germinal layer of cells, acellular laminated membrane of variable thickness and an outer host-produced layer of granulomatous adventitial reaction. Small vesicles called brood capsules bud internally from the germinal layer and produce multiple protoscolices by asexual division, where each protoscolex is able to form an adult worm if ingested by the definitive host (Eckert and Deplazes, 2004). The hydatid cysts develop slowly at a rate of 1–5 mm in diameter per year and although infections might be acquired in childhood, most cases become symptomatic in adulthood and can then be diagnosed. Most infections in humans are solitary (single cyst) (Eckert and Deplazes, 2004; Cornejo-Juárez et al., 2013), however, in certain occasions, 20–40% of individuals might have multiple cysts involving multiple organs (Cornejo-Juárez et al., 2013; Gattu and Bhasha, 2017). In humans and many other herbivores, the slowly growing hydatid cysts can attain a volume of several liters of hydatid fluid and contain thousands of protoscolices (Eckert and Deplazes, 2004).

3. Studies on cystic echinococcosis in Jordan

3.1. Retrospective and case report studies on (CE) in human patients

Information on the prevalence, incidence, and occurrence of CE in human in Jordan were obtained from surveys of individual hospitals medical reports of isolated cases, who underwent surgeries for hydatid cyst removal as well as from few retrospective seroepidemiological surveys (Tables 1 and 2).

Table 1 shows a comprehensive analysis of previously published studies on human patients who suffered from CE. The earliest documented CE cases (4 patients) were reported in 1966 by Khoury and Kamhawy, in which one patient out of the four had multiple operations due to recurrent hydatid cysts, 2 patients had complications due to multiple huge liver cysts and the last one was a child and died as a result of CE infection. Ten years later, another study reported 12 cases of pulmonary CE from the Military hospital in Amman (the capital of Jordan) with age distribution ranged from 12 to 70 years and most of them were males (Sliman, 1976). During the period of 1974–1977, CE was reported to mostly affect the liver and lungs in 50 patients (age

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