

Echinococcus granulosus genotypes in Iran: a systematic review

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Review Article

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Abstract

Cystic echinococcosis (CE) caused by *Echinococcus granulosus sensu lato* (*s.l.*) is a significant zoonosis, especially in developing countries of the Middle East, with many studies focusing on CE genotypes in Iran. We performed a systematic review to determine the exact status of *E. granulosus* genotypes in the country. We explored English (Pubmed, Scopus, ISI Web of Science and Science Direct) and Persian (Magiran, Iran Medex and Scientific Information Database) databases along with Google Scholar. Our review included 73 studies published prior to the end of 2015. In total, 2952 animal (intermediate and definitive) hosts were examined, and the prevalent genotypes comprised G1 (92.75%) and G6 (4.53%) in sheep, cattle, camels, goats and buffaloes; G3 (2.43%) in five herbivore hosts and dogs; G7 (0.2%) in sheep and goats; and G2 (0.06%) in dogs. G1 was mostly dominant in West Azerbaijan, whereas G3 and G6 were identified most frequently in the provinces of Isfahan and Fars, respectively. Regarding human CE infection, 340 cases were reported from Iran, with the identified genotypes G1 (n = 320), G6 (n = 13) and G3 (n = 7). Most CE-infected humans originated from Isfahan province (168 cases), whereas the lowest number of infected persons was noted in Kerman province (two cases). The information obtained from this systematic review is central to better understanding the biological and epidemiological characteristics of *E. granulosus s.l.* genotypes in Iran, leading to more comprehensive control strategies.

Introduction

Despite global community efforts to minimize parasitic helminthiasis in humans and animals in recent decades, numerous cases of such devastating diseases are still reported worldwide (Carmena & Cardona, 2014; Bartsch *et al.*, 2016; Cucher *et al.*, 2016; Khademvatan *et al.*, 2016; Saki *et al.*, 2017; Weatherhead *et al.*, 2017). *Echinococcus granulosus sensu lato* (*s.l.*), a cestode helminth belonging to the Taeniidae family, is the causative agent of a prevalent zoonotic disease, cystic echinococcosis (CE) (Rojas *et al.*, 2014). This tapeworm uses canids and herbivores/omnivores as definitive and intermediate hosts, respectively, and human infection occurs accidentally by ingestion of the eggs (Rokni, 2009). The disease in humans entails the development of a fluid-filled hydatid cyst, which localizes in the liver and lungs and, to a lesser extent, in the abdominal cavity, muscle, heart, bone and nervous system (Craig *et al.*, 2007). The disease causes impotency, disability and decreased work productivity in endemic territories, including Australia, New Zealand, China, Russia, South America, North Africa and the Middle East (Battelli, 2009; Shariatzadeh *et al.*, 2015). As a consequence of CE, 1–3.6 million disability-adjusted life years (DALYs) are missed globally; most of these cases occur in low-income countries (Budke *et al.*, 2006; Torgerson *et al.*, 2015). Given the numerous traditional animal husbandries and access of dogs to waste materials of abattoirs there, Iran has been considered a hyperendemic region (Dalimi *et al.*, 2002; Pour *et al.*, 2011; Khademvatan *et al.*, 2013). More recently, the weighted prevalence of hydatidosis in human and animal intermediate hosts in Iran reached 4.2% (95% confidence interval (CI) = 3.0–5.5%) and 15.6% (95% CI = 14.2–17.1%), respectively. The pooled prevalence of *E. granulosus* infection in definitive hosts totalled 23.6% (95% CI = 17.6–30.1%) (Khalkhali *et al.*, 2017). Human infection in Iran was mostly concentrated in the south, whereas the lowest prevalence rate was observed in central parts of the country (Khalkhali *et al.*, 2017). The annual monetary burden of CE in the country was estimated to be c. USD 232.3 million (Mobedi & Dalimi, 1994; Harandi *et al.*, 2012a).

Extensive intraspecies genetic diversity of CE has been recorded over a long period of time, and this condition may influence characteristics such as morphology, epidemiology, host specificity, infectivity and drug resistance (Carmena & Cardona, 2014). Four molecular

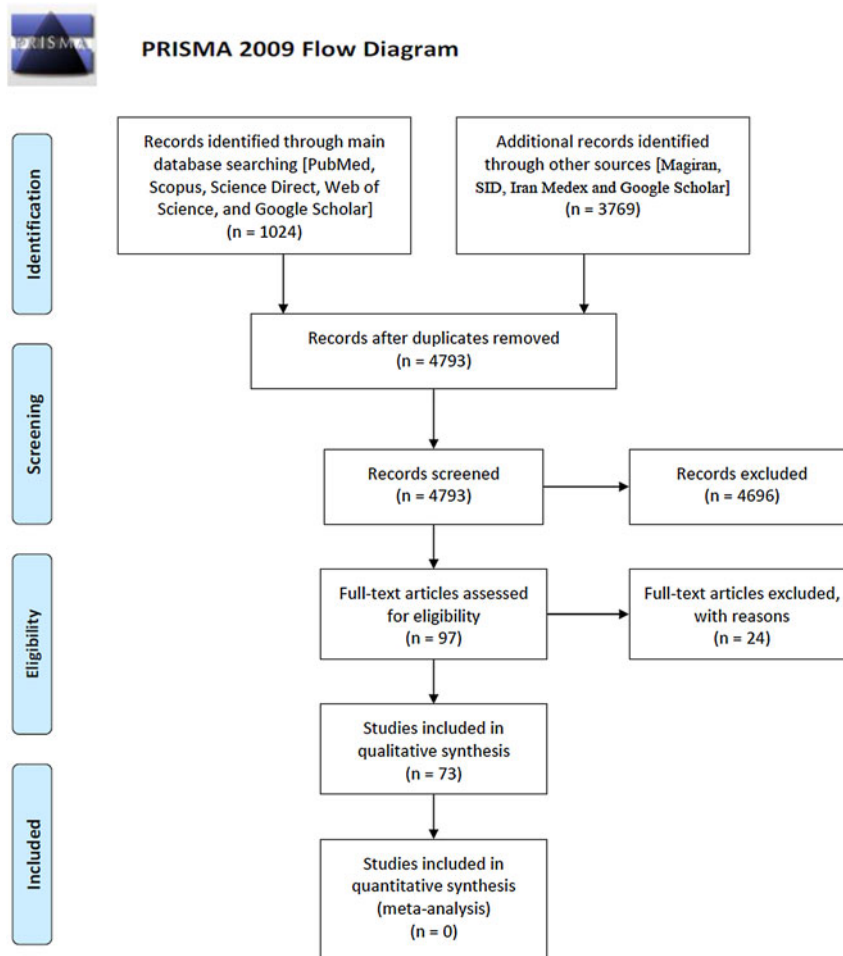


Fig. 1. PRISMA 2009 flow diagram.

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approaches – single-gene analysis using mitochondrial DNA, microsatellite markers for polymorphic DNA loci, full-genome exploration, and comparison of discrepancies among mitochondrial and nuclear DNA for species hybridization – have been used to categorize *Echinococcus* species into several genotypes (Ito & Budke, 2017). Most of our understanding in this area originates from the investigation of Bowles and colleagues into *cox1* and *nad1* mitochondrial genes (Bowles *et al.*, 1992). Accordingly, ten deduced strains of CE have been characterized and encompassed in a number of clades, including *E. granulosus sensu stricto* (s.s.) (G1–3), *E. equinus* (G4), *E. ortleppi* (G5) and *E. canadensis* (G6–10), and *E. felidis* (the lion strain) (Amer *et al.*, 2015). G1 and G2 are sheep strains, whereas G3 and G5 are buffalo and cattle strains, respectively. G4 is found in horses, G6 in camels, G7 in pigs and G8–10 in cervids (Rojas *et al.*, 2014). G1 genotype is the most commonly reported in human CE cases globally. Additionally, studies have reported that the subsequent strains are infective to humans (Grosso *et al.*, 2012). Host–parasite immunological interplay and cross transmission templates can justify the emergence of *Echinococcus* strains and their related genetic diversity (Bowles *et al.*, 1992; Thompson, 2013; Thompson & Jenkins, 2014). Detecting these genetic variations

in *E. granulosus s.l.* populations is significant for better understanding of various life cycles of CE in endemic regions of Iran and shedding light on more efficient prevention strategies, as well as diagnosis and treatment of CE (Shariatzadeh *et al.*, 2015).

Thus far, numerous papers have investigated CE genotypes in animal hosts and human cases in Iran. However, there is a lack of collective and processed data for systematic review. Accordingly, we performed a qualitative evaluation to clarify the status of CE genotypes in the country.

Methods

Search strategy

To unravel the genetic distribution of hydatid genotypes in Iran, a systematic review was designed on the basis of literature in English and Persian available online. Four English (PubMed, Scopus, Science Direct and ISI Web of Science) and three Persian (Scientific Information Database, Iran Medex and Magiran) databases were explored for published papers from inception to 31 December 2015, as was Google Scholar as a common, multilingual engine for both English and Persian terms. The

Table 1. Genotypes of *Echinococcus granulosus* identified in domestic natural hosts (intermediate and definitive) and humans in Iran.

Genotype	Intermediate natural host (a)	Definitive host (b)	No. of cases (a + b)	Human cases	Total (n)	References (a + b + c)
G1	Sheep, cattle, camels, goats, buffaloes		2738	320	3058	Harandi <i>et al.</i> , 2002; Rahimi <i>et al.</i> , 2007; Yousofi Darani <i>et al.</i> , 2007; Karimi & Dianatpour, 2008; Sharbatkhori <i>et al.</i> , 2009; Kia <i>et al.</i> , 2010; Gholami <i>et al.</i> , 2011; Pour <i>et al.</i> , 2011; Parsa <i>et al.</i> , 2011, 2012; Rostami Nejad <i>et al.</i> , 2011; Shahnazi <i>et al.</i> , 2011; Sharifiyazdi <i>et al.</i> , 2011; Yakhchali & Mardani, 2011, 2013; Hajjalilo <i>et al.</i> , 2012; Harandi <i>et al.</i> , 2012b; Hosseini <i>et al.</i> , 2012; Hosseinzadeh <i>et al.</i> , 2012; Nejad <i>et al.</i> , 2012; Rajabloo <i>et al.</i> , 2012; Sadri <i>et al.</i> , 2012; Dousti <i>et al.</i> , 2013; Hanifian <i>et al.</i> , 2013; Haniloo <i>et al.</i> , 2013; Khademvatan <i>et al.</i> , 2013; Moazeni <i>et al.</i> , 2013; Mobedi <i>et al.</i> , 2013; Sadjjadi <i>et al.</i> , 2013; Youssefi <i>et al.</i> , 2013; Eslami <i>et al.</i> , 2014; Nikmanesh <i>et al.</i> , 2014; Pestechian <i>et al.</i> , 2014; Sharafi <i>et al.</i> , 2014; Vahedi <i>et al.</i> , 2014; Fadakar <i>et al.</i> , 2015; Farhadi <i>et al.</i> , 2015; Rostami <i>et al.</i> , 2015; Spotin <i>et al.</i> , 2015; Oskouei <i>et al.</i> , 2016; Maldonado <i>et al.</i> , 2017
G2		Dogs	2		2	Parsa <i>et al.</i> , 2012; Sharafi <i>et al.</i> , 2014
G3	Sheep, cattle, camels, goats, buffaloes	Dogs	72	7	79	Sharbatkhori <i>et al.</i> , 2009; Pour <i>et al.</i> , 2011; Sharbatkhori <i>et al.</i> , 2011; Sharifiyazdi <i>et al.</i> , 2011; Hajjalilo <i>et al.</i> , 2012; Harandi <i>et al.</i> , 2012b; Parsa <i>et al.</i> , 2012; Dousti <i>et al.</i> , 2013; Hanifian <i>et al.</i> , 2013; Pezeshki <i>et al.</i> , 2013; Yakhchali & Mardani, 2013; Nikmanesh <i>et al.</i> , 2014; Pestechian <i>et al.</i> , 2014; Sharafi <i>et al.</i> , 2014; Babazadeh <i>et al.</i> , 2015; Farhadi <i>et al.</i> , 2015; Rostami <i>et al.</i> , 2015; Shariatzadeh <i>et al.</i> , 2015; Oskouei <i>et al.</i> , 2016
G6	Sheep, cattle, camels, goats, buffaloes		134	13	147	Harandi <i>et al.</i> , 2002; Karimi & Dianatpour, 2008; Sharbatkhori <i>et al.</i> , 2010; Rostami Nejad <i>et al.</i> , 2011; Shahnazi <i>et al.</i> , 2011; Sharifiyazdi <i>et al.</i> , 2011; Hajjalilo <i>et al.</i> , 2012; Harandi <i>et al.</i> , 2012b; Hosseinzadeh <i>et al.</i> , 2012; Nejad <i>et al.</i> , 2012; Rajabloo <i>et al.</i> , 2012; Sadjjadi <i>et al.</i> , 2013; Eslami <i>et al.</i> , 2014; Nikmanesh <i>et al.</i> , 2014; Pestechian <i>et al.</i> , 2014; Sharafi <i>et al.</i> , 2014; Rostami <i>et al.</i> , 2015; Shariatzadeh <i>et al.</i> , 2015; Spotin <i>et al.</i> , 2015
G7	Sheep, goats		6		6	Hosseinzadeh <i>et al.</i> , 2012; Fadakar <i>et al.</i> , 2015
<i>Total</i>			2952	340	3292	

current review was conducted using the following Medical Subject Headings (MeSH) terms: ‘*Echinococcus granulosus*’, ‘*Echinococcus*’, ‘Echinococcosis’, ‘Hydatid’, ‘Hydatic’, ‘Iran’, ‘Prevalence’, ‘Epidemiology’ and ‘Genotype’, alone or combined together with ‘OR’ or/and ‘AND’ operators.

Study selection and data extraction

Eligibility of studies and inclusion criteria were checked carefully by two independent reviewers (S. Khademvatan and S. Aryamand). Contradiction among studies was obviated by discussion and consensus (Foroutan-Rad *et al.*, 2016a, b; Majidiani *et al.*, 2016; Foroutan *et al.*, 2017a, b, c; Khademvatan *et al.*, 2017; Khalkhali *et al.*, 2017; Maleki *et al.*, 2017). The inclusion criteria were as follows: (1) peer-reviewed original research papers; (2) cross-sectional studies based on various polymerase chain reaction techniques and investigating the genotypes of *E. granulosus* in Iran; (3) published in English or Persian; (4) published online from inception to 31 December 2015; (5) full-text articles were available. Papers that failed to meet these criteria were excluded. The required data were collected accurately using a data extraction form, on the basis of the first author, province, geographical region (north, south, east, west, centre), infected organ, genotypes (G1, G2, G3, G4, G5, G6, G7, G8, G9, G10), intermediate and definitive hosts, human cases, type of diagnostic method and the DNA/RNA fragment used in detection. The

review was conducted in accordance with PRISMA (preferred reporting items for systematic reviews and meta-analyses) guidelines (Moher *et al.*, 2010). ArcGIS (<http://www.esri.com>) was used for mapping the geographical distribution of various genotypes of *E. granulosus* in Iran.

Results

In total, 73 of 4793 studies met the inclusion criteria and were included in the systematic review (fig. 1). Literature search results and study properties (species, genotypes, animal intermediate host, definitive host, number of animal and human cases) are presented in table 1. Table 2 and supplementary fig. S1 show the geographical diversification of genotypes detected in different provinces in Iran. The number of each genotype in each of the various hosts is shown in table 3.

Intermediate and definitive animal hosts

In total, 2952 animal (intermediate and definitive) hosts were examined for cystic echinococcosis. Five *E. granulosus* s.l. genotypes exist in Iran (G1, G2, G3, G6, G7), and five livestock species (sheep, goats, cattle, buffaloes, camels) were affected by CE (table 1). With the exception of G7, which is localized in Khorasan province, eastern Iran, other genotypes were detected mostly in central and western parts of the country

Table 2. Numbers of *E. granulosus s.l.* genotypes identified in various regions of Iran.

Region	Province	G1	G6	G3	G2	G7
North-east	Khorasan	74	–	–	–	–
North	Gilan	2	–	–	–	–
	Golestan	95	10	–	–	–
	Mazandaran	140	–	–	–	–
North-west	West Azerbaijan	818	–	2	–	–
	East Azerbaijan	91	1	2	–	–
	Ardabil	59	–	6	–	–
	Zanjan	168	–	4	–	–
Centre	Isfahan	603	50	47	–	–
	Tehran	99	1	3	–	–
	Semnan	45	15	–	–	–
West	Lorestan	163	–	3	2	–
South-west	Khuzestan	421	1	1	–	6
	Kohgiluyeh and Boyer-Ahmad	93	–	–	–	–
	Chaharmahal va Bakhtiari	30	–	–	–	–
South	Fars	97	57	–	–	–
South-east	Kerman	60	12	11	–	–
East	–	–	–	–	–	–
<i>Total</i>		3058	147	79	2	6

(supplementary fig. S1). Molecular studies revealed that *E. granulosus s.s.* clade (G1–3) was involved in most cases of infection, among which the G1 genotype was the most diverse and prevalent, with 2738 of 3058 (92%) cases in animal hosts, and dominant in 17 provinces, particularly in West Azerbaijan (table 2). The geographical distribution and involvement of various intermediate hosts demonstrates why G1 is the most abundant in the country. Results also revealed that the dog–sheep cycle of CE is widespread in most parts of Iran, indicating that G1 is viable for transmission. Most G3 and G6 cases were reported from Isfahan and Fars provinces, respectively (table 2). Animal host involvements of each recognized genotype in Iran are as follows: G1 (92.75%) and G6 (4.53%) in sheep, cattle, camels, goats and buffaloes; G3 (2.43%) in five herbivore hosts and dogs; G2 (0.06%) in dogs; and G7 (0.2%) in sheep and goats (table 3). In one study, genotype co-infection with G1, G3 and G6 was discerned. With respect to G2 and G7 genotypes, more sequencing data from various animal hosts (intermediate and definitive),

particularly from provinces with fewer studies, are required to reach a rational consensus on the host range and geographical distribution of these genotypes. The findings suggest that special attention be paid to water buffaloes in subsequent works, as they may play a role in lifecycle maintenance of G1, G3 and G6 strains in Iran. Some characteristics of the G6 genotype are significant for CE diagnosis and control strategies (Kamenetzky *et al.*, 2005; Chow *et al.*, 2008; Muzulin *et al.*, 2008). No sequencing information exists for the G4 genotype in Iran, necessitating molecular studies in horses. No molecular evidence from G8–10 genotypes has been reported from the country.

In general, in the case of neighbouring countries there was a low diversity in the animal hosts examined and subsequently in CE genotypes isolated, with most studies focused on *E. granulosus s.s.* (Utuk *et al.*, 2008; Latif *et al.*, 2010; Simsek *et al.*, 2011; Eryıldız & Şakru, 2012; Hama *et al.*, 2012; Hama & Shareef, 2016; Hasan *et al.*, 2016; Gökpinar *et al.*, 2017; Hassan *et al.*, 2017). With some exceptions (Al-Qaoud *et al.*, 2003; Trachsel

Table 3. Numbers of *E. granulosus s.l.* genotypes identified in animal and human hosts in Iran.

	Sheep	Cattle	Goats	Camels	Buffaloes	Dogs	Humans	Total
G1	1362	525	613	173	52	13	320	3058
G2	–	–	–	–	–	2	–	2
G3	1	36	10	20	1	4	7	79
G6	2	54	9	63	–	6	13	147
G7	–	–	–	–	–	6	–	6
<i>Total</i>	1365	615	632	256	53	31	340	3292

et al., 2007; Ziadinov *et al.*, 2008), the strains identified in definitive hosts in Iran are partly identical to detected genotypes in adjacent countries.

Human cases

In total, 340 cases of CE in humans have been reported, with sequencing data, from Iran. Major *E. granulosus* genotypes in infected individuals include G1 (n = 320) and G3 (n = 7) as *E. granulosus s.s.*, and G6 (n = 13) as *E. canadensis* (tables 1 and 3). Alongside the exclusive G1 genotype, which is dominant globally, G6 is the most prevalent clade in human infections in Iran, similar to recent data from South American countries (Cucher *et al.*, 2016). Based on the study of Sadjjadi *et al.* (2013) in Iran, *E. canadensis* is responsible for brain infections, suggesting an alternative predilection site to the liver. Consequently, nationwide research is required to clarify the exact epidemiological status and biological behaviour of this clade in Iran. Based on our results, the highest and lowest incidences of human CE infections were in Isfahan (168 cases) and Kerman (two cases) provinces, respectively. Considering the capability of cattle and camels to harbour multiple genotypes (table 1), these animals probably play a central role in preserving the CE life cycle and the risk of human transmission, particularly camels in central arid parts of Iran, where they are possibly involved in G6 environmental maintenance. The absence of G7 (pig strain) in human cases may be partially attributed to the lack of pig breeding in Islamic culture. Human cases in Afghanistan and Pakistan have been discerned as the G1 strain, whereas more diverse CE genotypes have been isolated from human subjects in Iraq and Turkey than in Iran (Rojas *et al.*, 2014).

Discussion

Cystic echinococcosis is an important neglected parasitic disease worldwide. In a review of the current situation of echinococcosis in Asia, Ito & Budke (2017) discussed various aspects of CE throughout the continent but provided no data for Iran. The current work and a previously published meta-analysis (Khalkhali *et al.*, 2017) appropriately report up-to-date information regarding the epidemiology of CE in Iran. Several strains of CE with specific epidemiological and biological emphases have been categorized in various clades, including the following: *E. granulosus s.s.* (G1–3), *E. equinus* (G4), *E. ortleppi* (G5) and *E. canadensis* (G6–10), and *E. felidis* (the lion strain). More studies using sophisticated molecular tools are a requisite to revealing more genotype diversity and their respective hosts in Iran. This paper reviewed works featuring sequencing discrimination of CE genotypes in natural hosts and human cases in Iran. Reportedly, G6 was the second most abundant genotype in all hosts, after G1. Regarding antigenic variations in EG95-related proteins of G1 and G6, studies should focus on the diagnosis, chemotherapy and pathogenicity of the G6 strain (Alvarez Rojas *et al.*, 2013). The lack of human cases of the G4 genotype may be attributable to the requirement of additional host samples and sequencing information and/or the non-infectious condition of the G4 genotype for human hosts. A wide range of animals were proven to be involved in the ecological maintenance of pastoral and sylvatic life cycles of CE. Our review was confined to published literature, and therefore our findings may not provide a full representation of CE genotypes throughout Iran. In conclusion, the data obtained from

this systematic review could benefit local and nationwide CE control initiatives, such as effective CE vaccines for dogs and livestock, improved diagnostic methods for humans and definitive hosts, efficient treatment options and development of well-structured mathematical models for better evaluation of cost-effective interventions.

Supplementary material. To view supplementary material for this article, please visit <https://doi.org/10.1017/S0022149X18000275>

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Conflict of interest. None.

Ethical standards. This study was approved by the Ethical Committee of Urmia University of Medical Sciences, Urmia, Iran (IR.UMSU.REC.1395.511).

Author contributions. S. Khademvatan and M. Foroutan conceived the study; S. Khademvatan and S. Aryamand designed the study protocol; M. Foroutan and S. Khademvatan searched the literatures; S. Aryamand extracted the data; H. Khalkhali analysed and interpreted the data; H. Majidiani wrote the manuscript; S. Khademvatan, H. Majidiani, M. Foroutan and K. Hazrati Tappeh critically revised the manuscript. All authors read and approved the final manuscript.

References

- Al-Qaoud KM, Abdel-Hafez SK and Craig PS (2003) Canine echinococcosis in northern Jordan: increased prevalence and dominance of sheep/dog strain. *Parasitology Research* **90**, 187–191.
- Alvarez Rojas CA, Gauci CG and Lightowlers MW (2013) Antigenic differences between the EG95-related proteins from *Echinococcus granulosus* G1 and G6 genotypes: implications for vaccination. *Parasite Immunology* **35**, 99–102.
- Amer S, Helal IB, Kamau E, Feng Y and Xiao L (2015) Molecular characterization of *Echinococcus granulosus* sensu lato from farm animals in Egypt. *PLoS ONE* **10**(3), e0118509.
- Babazadeh M, Sharifiyazdi H, Moazeni M, Gorjipour S and Heidari M (2015) Molecular characterization of a new microvariant of the G3 genotype for *Echinococcus granulosus* in water buffalo in Iran. *Veterinary Research Forum* **6**, 83–87.
- Bartsch SM, Hotez PJ, Asti L, Zapf KM, Bottazzi ME, Diemert DJ and Lee BY (2016) The global economic and health burden of human hookworm infection. *PLoS Neglected Tropical Diseases* **10**(9), e0004922.
- Battelli G (2009) Echinococcosis: costs, losses and social consequences of a neglected zoonosis. *Veterinary Research Communications* **33**, 47–52.
- Bowles J, Blair D and McManus DP (1992) Genetic variants within the genus *Echinococcus* identified by mitochondrial DNA sequencing. *Molecular and Biochemical Parasitology* **54**, 165–173.
- Budke CM, Deplazes P and Torgerson PR (2006) Global socioeconomic impact of cystic echinococcosis. *Emerging Infectious Diseases* **12**, 296–303.
- Carmena D and Cardona GA (2014) Echinococcosis in wild carnivorous species: epidemiology, genotypic diversity, and implications for veterinary public health. *Veterinary Parasitology* **202**, 69–94.
- Chow C, Gauci CG, Vural G, Jenkins DJ, Heath DD, Rosenzvit MC, Harandi MF and Lightowlers MW (2008) *Echinococcus granulosus*: variability of the host-protective EG95 vaccine antigen in G6 and G7 genotypic variants. *Experimental Parasitology* **119**, 499–505.
- Craig PS, McManus DP, Lightowlers MW *et al.* (2007) Prevention and control of cystic echinococcosis. *The Lancet Infectious Diseases* **7**, 385–394.
- Cucher MA, Macchiaroli N, Baldi G *et al.* (2016) Cystic echinococcosis in South America: systematic review of species and genotypes of *Echinococcus*

- granulosus sensu lato* in humans and natural domestic hosts. *Tropical Medicine and International Health* **21**, 166–175.
- Dalimi A, Motamedi G, Hosseini M, Mohammadian B, Malaki H, Ghamari Z and Ghaffarifar F** (2002) Echinococcosis/hydatidosis in western Iran. *Veterinary Parasitology* **105**, 161–171.
- Dousti M, Abdi J, Bakhtiyari S, Mohebbali M, Mirhendi S and Rokni M** (2013) Genotyping of hydatid cyst isolated from human and domestic animals in Ilam Province, Western Iran using PCR-RFLP. *Iranian Journal of Parasitology* **8**, 47–52.
- Eryildiz C and Şakru N** (2012) Molecular characterization of human and animal isolates of *Echinococcus granulosus* in the Thrace Region, Turkey. *Balkan Medical Journal* **29**, 261–267.
- Eslami A, Shayan P and Bokaei S** (2014) Morphological and genetic characteristics of the liver hydatid cyst of a donkey with Iran origin. *Iranian Journal of Parasitology* **9**, 302–310.
- Fadakar B, Tabatabaei N, Borji H and Naghibi A** (2015) Genotyping of *Echinococcus granulosus* from goats and sheep indicating G7 genotype in goats in the northeast of Iran. *Veterinary Parasitology* **214**, 204–207.
- Farhadi M, Fazaeli A and Haniloo A** (2015) Genetic characterization of livestock and human hydatid cyst isolates from northwest Iran, using the mitochondrial *cox1* gene sequence. *Parasitology Research* **114**, 4363–4370.
- Foroutan-Rad M, Khademvatan S, Majidiani H, Aryamand S, Rahim F and Malehi AS** (2016a) Seroprevalence of *Toxoplasma gondii* in the Iranian pregnant women: a systematic review and meta-analysis. *Acta Tropica* **158**, 160–169.
- Foroutan-Rad M, Majidiani H, Dalvand S, Daryani A, Kooti W, Saki J, Hedayati-Rad F and Ahmadpour E** (2016b) Toxoplasmosis in blood donors: a systematic review and meta-analysis. *Transfusion Medicine Reviews* **30**, 116–122.
- Foroutan M, Dalvand S, Daryani A, Ahmadpour E, Majidiani H, Khademvatan S and Abbasi E** (2017a) Rolling up the pieces of a puzzle: systematic review and meta-analysis of the prevalence of toxoplasmosis in Iran. *Alexandria Journal of Medicine* (in press).
- Foroutan M, Dalvand S, Khademvatan S, Majidiani H, Khalkhali H, Masoumifard S and Shamsaddin G** (2017b) A systematic review and meta-analysis of the prevalence of *Leishmania* infection in blood donors. *Transfusion and Apheresis Science* **56**, 544–551.
- Foroutan M, Khademvatan S, Majidiani H, Khalkhali H, Hedayati-Rad F, Khashaveh S and Mohammadzadeh H** (2017c) Prevalence of *Leishmania* species in rodents: a systematic review and meta-analysis in Iran. *Acta Tropica* **172**, 164–172.
- Gholami S, Sosarai M, Fakhari M, Sharif M and Daryani A** (2011) Genotype identification of *Echinococcus granulosus* from paraffin-embedded tissues of hydatid cysts isolated from human by PCR-RFLP. *Journal of Mazandaran University of Medical Sciences* **21**, 10–19.
- Gökpinar S, Değirmenci R and Yıldız K** (2017) Genotyping of *Echinococcus granulosus* obtained from cattle slaughtered in Kirikkale Province. *Ankara Üniversitesi Veteriner Fakültesi Dergisi* **64**, 51–54.
- Grosso G, Gruttadauria S, Biondi A, Marventano S and Mistretta A** (2012) Worldwide epidemiology of liver hydatidosis including the Mediterranean area. *World Journal of Gastroenterology* **18**, 1425–1437.
- Hajjalilo E, Harandi MF, Sharbatkhori M, Mirhendi H and Rostami S** (2012) Genetic characterization of *Echinococcus granulosus* in camels, cattle and sheep from the south-east of Iran indicates the presence of the G3 genotype. *Journal of Helminthology* **86**, 263–270.
- Hama AA and Shareef OH** (2016) Morphological and morphometric study of *Echinococcus granulosus* (metacestode) in Sulaimani Province/Kurdistan Region, Iraq. *Kurdistan Journal of Applied Research* **1**, 71–76.
- Hama AA, Mero WM and Jubrael JM** (2012) Molecular characterization of *E. granulosus*, first report of sheep strain in Kurdistan-Iraq. In *2nd International Conference on Ecological, Environmental and Biological Sciences (EEBS 2012)*, 13th–14th October.
- Hanifian H, Diba K, Hazrati Tappeh K, Mohammadzadeh H and Mahmoudlou R** (2013) Identification of *Echinococcus granulosus* strains in isolated hydatid cyst specimens from animals by PCR-RFLP method in West Azerbaijan-Iran. *Iranian Journal of Parasitology* **8**, 376–381.
- Haniloo A, Farhadi M, Fazaeli A and Nourian N** (2013) Genotype characterization of hydatid cysts isolated from Zanjan using PCR-RFLP technique. *Journal of Zanjan University of Medical Sciences and Health Services* **21**, 57–65.
- Harandi MF, Budke CM and Rostami S** (2012a) The monetary burden of cystic echinococcosis in Iran. *PLoS Neglected Tropical Diseases* **6**(11), e1915.
- Harandi MF, Hajjalilo E and Shokouhi M** (2012b) Larval hook length measurement for differentiating G1 and G6 genotypes of *Echinococcus granulosus sensu lato*. *Türkiye Parazitoloji Dergisi* **36**, 215–218.
- Harandi MF, Hobbs RP, Adams PJ, Mobedi I, Morgan-Ryan UM and Thompson RCA** (2002) Molecular and morphological characterization of *Echinococcus granulosus* of human and animal origin in Iran. *Parasitology* **125**, 367–373.
- Hasan HF, Fadhil MH and Fadhil ZH** (2016) Molecular characterization of *Echinococcus granulosus* isolated from human and domestic animals in Kirkuk, Iraq. *Animal Research International* **13**.
- Hassan ZI, Mero WM, Casulli A, Interisano M and Boufana B** (2017) Epidemiological study of cystic echinococcosis in sheep, cattle and goats in Erbil Province. *Science Journal of University of Zakho* **4**, 43–55.
- Hosseini SH, Pour AA and Shayan P** (2012) Morphological characteristics of *Echinococcus granulosus* derived from buffalo in Iran. *Parasitology* **139**, 103–109.
- Hosseinzadeh S, Fazeli M, Hosseini A and Shekarforoush SS** (2012) Molecular characterization of *Echinococcus granulosus* in south of Iran. *Open Journal of Veterinary Medicine* **2**, 201–206.
- Ito A and Budke CM** (2017) The echinococcoses in Asia: the present situation. *Acta Tropica* **176**, 11–21.
- Kamenetzky L, Muzulin PM, Gutierrez AM, Angel SO, Zaha A, Guarnera EA and Rosenzvit MC** (2005) High polymorphism in genes encoding antigen B from human infecting strains of *Echinococcus granulosus*. *Parasitology* **131**, 805–815.
- Karimi A and Dianatpour R** (2008) Genotypic and phenotypic characterization of *Echinococcus granulosus* of Iran. *Biotechnology* **7**, 757–762.
- Khademvatan S, Foroutan M, Hazrati-Tappeh K, Dalvand S, Khalkhali H, Masoumifard S and Hedayati-Rad F** (2017) Toxoplasmosis in rodents: a systematic review and meta-analysis in Iran. *Journal of Infection and Public Health* **10**, 487–493.
- Khademvatan S, Salmanzadeh S, Foroutan-Rad M and Ghomeshi M** (2016) Elimination of urogenital schistosomiasis in Iran: past history and the current situation. *Parasitology* **143**, 1390–1396.
- Khademvatan S, Yousefi E, Rafiei A, Rahdar M and Saki J** (2013) Molecular characterization of livestock and human isolates of *Echinococcus granulosus* from south-west Iran. *Journal of Helminthology* **87**, 240–244.
- Khalkhali H, Foroutan M, Khademvatan S, Majidiani H, Aryamand S, Khezri P and Aminpour A** (2017) Prevalence of cystic echinococcosis in Iran: a systematic review and meta-analysis. *Journal of Helminthology* (in press).
- Kia EB, Rahimi H, Sharbatkhori M, Talebi A, Harandi MF and Mirhendi H** (2010) Genotype identification of human cystic echinococcosis in Isfahan, central Iran. *Parasitology Research* **107**, 757–760.
- Latif AA, Tanveer A, Maqbool A, Siddiqi N, Kyaw-Tanner M and Traub RJ** (2010) Morphological and molecular characterisation of *Echinococcus granulosus* in livestock and humans in Punjab, Pakistan. *Veterinary Parasitology* **170**, 44–49.
- Majidiani H, Dalvand S, Daryani A, de la Luz Galvan-Ramirez M and Foroutan-Rad M** (2016) Is chronic toxoplasmosis a risk factor for diabetes mellitus? A systematic review and meta-analysis of case-control studies. *The Brazilian Journal of Infectious Diseases* **20**, 605–609.
- Maldonado LL, Assis J, Araújo FMG et al.** (2017) The *Echinococcus canadensis* (G7) genome: a key knowledge of parasitic plathyhelminth human diseases. *BMC Genomics* **18**, 204.
- Maleki B, Khorshidi A, Gorgipour M, Mirzapour A, Majidiani H and Foroutan M** (2017) Prevalence of *Toxocara* spp. eggs in soil of public areas in Iran: a systematic review and meta-analysis. *Alexandria Journal of Medicine* (in press).
- Moazeni M, Taghipour S, Abolhasani M, Hashemzadeh M, Zarean E and Darani HY** (2013) Molecular characterization of the human and sheep hydatid cyst strains in Chaharmahal va Bakhtiari province of Iran using

- restriction fragment length polymorphism (PCR RFLP). *Applied Cell Biology* 2, 78–83.
- Mobedi I and Dalimi A** (1994) Epidemiology of hydatid cyst in Iran and world. *Tehran: Moghaddam Publication*, 132–147.
- Mobedi I, Zare-Bidaki M, Siavashi M, Naddaf S, Kia E and Mahmoudi M** (2013) Differential detection of *Echinococcus* spp. copro-DNA by nested-PCR in domestic and wild definitive hosts in Moghan Plain, Iran. *Iranian Journal of Parasitology* 8, 107–113.
- Moher D, Liberati A, Tetzlaff J, Altman DG and the PRISMA Group** (2010) Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *International Journal of Surgery* 8, 336–341.
- Muzulin PM, Kamenetzky L, Gutierrez AM, Guarnera EA and Rosenzvit MC** (2008) *Echinococcus granulosus* antigen B gene family: further studies of strain polymorphism at the genomic and transcriptional levels. *Experimental Parasitology* 118, 156–164.
- Nejad MR, Taghipour N, Nochi Z, Mojarad EN, Mohebbi SR, Harandi MF and Zali MR** (2012) Molecular identification of animal isolates of *Echinococcus granulosus* from Iran using four mitochondrial genes. *Journal of Helminthology* 86, 485–492.
- Nikmanesh B, Mirhendi H, Ghalavand Z, Alebouyeh M, Sharbatkhori M, Kia E, Mohebbi M, Eghbali M and Rokni MB** (2014) Genotyping of *Echinococcus granulosus* isolates from human clinical samples based on sequencing of mitochondrial genes in Iran, Tehran. *Iranian Journal of Parasitology* 9, 20–27.
- Oskouei MM, Mehrabani NG, Miahipour A and Fallah E** (2016) Molecular characterization and sequence analysis of *Echinococcus granulosus* from sheep isolates in East Azerbaijan province, northwest of Iran. *Journal of Parasitic Diseases* 40, 785–790.
- Parsa F, Haghpanah B, Pestecheian N and Salehi M** (2011) Molecular epidemiology of *Echinococcus granulosus* strains in domestic herbivores of Lorestan, Iran. *Jundishapur Journal of Microbiology* 4, 123–130.
- Parsa F, Harandi MF, Rostami S and Sharbatkhori M** (2012) Genotyping *Echinococcus granulosus* from dogs from Western Iran. *Experimental Parasitology* 132, 308–312.
- Pestecheian N, Safa AH, Tadjedini M, Rostami-Nejad M, Mousavi M, Yousofi H and Javanmard SH** (2014) Genetic diversity of *Echinococcus granulosus* in center of Iran. *The Korean Journal of Parasitology* 52, 413–418.
- Pezeshki A, Akhlaghi L, Sharbatkhori M, Razmjou E, Oormazdi H, Mohebbi M and Meamar AR** (2013) Genotyping of *Echinococcus granulosus* from domestic animals and humans from Ardabil Province, northwest Iran. *Journal of Helminthology* 87, 387–391.
- Pour AA, Hosseini SH and Shayan P** (2011) Comparative genotyping of *Echinococcus granulosus* infecting buffalo in Iran using *cox1* gene. *Parasitology Research* 108, 1229–1234.
- Rahimi HR, Kia EB, Mirhendi SH, Talebi A, Harandi MF, Jalali-Zand N and Rokni MB** (2007) A new primer pair in ITS1 region for molecular studies on *Echinococcus granulosus*. *Iranian Journal of Public Health* 36, 45–49.
- Rajabloo M, Hosseini SH and Jalousian F** (2012) Morphological and molecular characterisation of *Echinococcus granulosus* from goat isolates in Iran. *Acta Tropica* 123, 67–71.
- Rojas CAA, Romig T and Lightowlers MW** (2014) *Echinococcus granulosus sensu lato* genotypes infecting humans – review of current knowledge. *International Journal for Parasitology* 44, 9–18.
- Rokni M** (2009) Echinococcosis/hydatidosis in Iran. *Iranian Journal of Parasitology* 4, 1–16.
- Rostami Nejad M, Nazemalhosseini Mojarad E, Taghipour N, Nochi Z, Cheraghpour K, Dabiri H, Mohebbi SR, Noorinayer B and Zali MR** (2011) Molecular determination of *Echinococcus granulosus* isolated from hydatid cyst using mitochondrial *atp6* gene. *Journal of Gorgan University of Medical Sciences* 13, 61–67.
- Rostami S, Torbaghan SS, Dabiri S, Babaei Z, Mohammadi MA, Sharbatkhori M and Harandi MF** (2015) Genetic characterization of *Echinococcus granulosus* from a large number of formalin-fixed, paraffin-embedded tissue samples of human isolates in Iran. *The American Journal of Tropical Medicine and Hygiene* 92, 588–594.
- Sadjjadi SM, Mikaeili F, Karamian M, Maraghi S, Sadjjadi FS, Shariat-Torbaghan S and Kia EB** (2013) Evidence that the *Echinococcus granulosus* G6 genotype has an affinity for the brain in humans. *International Journal for Parasitology* 43, 875–877.
- Sadri A, Moshfe A, Doosti A, Ansari H, Abidi H and Ghorbani Dalini S** (2012) Characterization of isolated hydatid cyst from slaughtered livestock in Yasuj industrial slaughterhouse by PCR-RFLP. *Armaghane Danesh* 17, 243–252.
- Saki J, Khademvatan S, Foroutan-Rad M and Gharibzadeh M** (2017) Prevalence of intestinal parasitic infections in Haftkel County, southwest of Iran. *International Journal of Infection* 4, e15593. doi: 10.5812/iji.15593.
- Shahnazi M, Hejazi H, Salehi M and Andalib AR** (2011) Molecular characterization of human and animal *Echinococcus granulosus* isolates in Isfahan, Iran. *Acta Tropica* 117, 47–50.
- Sharafi SM, Rostami-Nejad M, Moazeni M, Yousefi M, Saneie B, Hosseini-Safa A and Yousofi-Darani H** (2014) *Echinococcus granulosus* genotypes in Iran. *Gastroenterology and Hepatology from Bed to Bench* 7, 82–88.
- Sharbatkhori M, Harandi MF, Mirhendi H, Hajjalilo E and Kia EB** (2011) Sequence analysis of *cox1* and *nad1* genes in *Echinococcus granulosus* G3 genotype in camels (*Camelus dromedarius*) from central Iran. *Parasitology Research* 108, 521–527.
- Sharbatkhori M, Mirhendi H, Harandi MF, Rezaeian M, Mohebbi M, Eshraghian M, Rahimi H and Kia EB** (2010) *Echinococcus granulosus* genotypes in livestock of Iran indicating high frequency of G1 genotype in camels. *Experimental Parasitology* 124, 373–379.
- Sharbatkhori M, Mirhendi H, Jex AR, Pangasa A, Campbell BE, Kia EB, Eshraghian MR, Harandi MF and Gasser RB** (2009) Genetic categorization of *Echinococcus granulosus* from humans and herbivorous hosts in Iran using an integrated mutation scanning-phylogenetic approach. *Electrophoresis* 30, 2648–2655.
- Shariatzadeh SA, Spotin A, Gholami S, Fallah E, Hazratian T, Mahami-Oskouei M, Montazeri F, Moslemzadeh HR and Shahbazi A** (2015) The first morphometric and phylogenetic perspective on molecular epidemiology of *Echinococcus granulosus sensu lato* in stray dogs in a hyperendemic Middle East focus, northwestern Iran. *Parasites & Vectors* 8, 409.
- Sharifiyazdi H, Oryan A, Ahmadnia S and Valinezhad A** (2011) Genotypic characterization of Iranian camel (*Camelus dromedarius*) isolates of *Echinococcus granulosus*. *Journal of Parasitology* 97, 251–255.
- Simsek S, Balkaya I, Ciftci AT and Utuk AE** (2011) Molecular discrimination of sheep and cattle isolates of *Echinococcus granulosus* by SSCP and conventional PCR in Turkey. *Veterinary Parasitology* 178, 367–369.
- Spotin A, Gholami S, Nasab AN, Fallah E, Oskouei MM, Semnani V, Shariatzadeh SA and Shahbazi A** (2015) Designing and conducting in silico analysis for identifying of *Echinococcus* spp. with discrimination of novel haplotypes: an approach to better understanding of parasite taxonomic. *Parasitology Research* 114, 1503–1509.
- Thompson RCA and Jenkins DJ** (2014) *Echinococcus* as a model system: biology and epidemiology. *International Journal for Parasitology* 44, 865–877.
- Thompson RCA** (2013) Parasite zoonoses and wildlife: one health, spillover and human activity. *International Journal for Parasitology* 43, 1079–1088.
- Torgerson PR, Devleeschauwer B, Praet N et al.** (2015) World Health Organization estimates of the global and regional disease burden of 11 foodborne parasitic diseases, 2010: a data synthesis. *PLoS Medicine* 12, e1001920. doi: 10.1371/journal.pmed.1001920.
- Trachsel D, Deplazes P and Mathis A** (2007) Identification of taeniid eggs in the faeces from carnivores based on multiplex PCR using targets in mitochondrial DNA. *Parasitology* 134, 911–920.
- Utuk AE, Simsek S, Koroglu E and McManus DP** (2008) Molecular genetic characterization of different isolates of *Echinococcus granulosus* in east and southeast regions of Turkey. *Acta Tropica* 107, 192–194.
- Vahedi A, Mahdavi M, Ghazanchaei A and Shokouhi B** (2014) Genotypic characteristics of hydatid cysts isolated from humans in East Azerbaijan Province (2011–2013). *Journal of Analytical Research in Clinical Medicine* 2, 152–157.
- Weatherhead JE, Hotez PJ and Mejia R** (2017) The global state of helminth control and elimination in children. *Pediatric Clinics of North America* 64, 867–877.
- Yakhchali M and Mardani K** (2011) Study on *Echinococcus granulosus* genotype diversity in domestic cycle using nucleotide sequence of *nda-1* gene. *Iran Veterinary Journal* 7, 63–69.

- Yakhchali M and Mardani K** (2013) A study on *Echinococcus granulosus* strains using nucleotide sequence of CO-1 gene by PCR-RFLP technique in West Azarbaijan Province, Iran. *Urmia Medical Journal* **23**, 792–798.
- Yousofi Darani H, Hashemzadeh CM, Aliyari Z, Zebardast N and Farokhi E** (2007) Molecular characterization of the strains cause sheep-hydatid cyst, in Chaharmahal va Bakhtiary Province using restriction fragment length polymorphism. *Journal of Shahrekord University of Medical Sciences* **9**.
- Youssefi MR, Tabaripour R, Omrani VF, Spotin A and Esfandiari B** (2013) Genotypic characterization of *Echinococcus granulosus* in Iranian goats. *Asian Pacific Journal of Tropical Disease* **3**, 362–366.
- Ziadinov I, Mathis A, Trachsel D, Rysmukhambetova A, Abdyjaparov TA, Kuttubaev OT, Deplazes P and Torgerson PR** (2008) Canine echinococcosis in Kyrgyzstan: using prevalence data adjusted for measurement error to develop transmission dynamics models. *International Journal for Parasitology* **38**, 1179–1190.