



## Human Cystic Echinococcosis in Different Geographical Zones of Iran: An Observational Study during 1995–2014

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### Abstract

**Background:** Cystic Echinococcosis (CE) is a serious zoonotic parasitic disease in Iran. This study aimed to show the trend of the confirmed disease from 1995 to 2014 and to describe some of epidemiological aspects of the disease in Iran.

**Methods:** This retrospective study has been designed based on data collected from 8518 cases of CE among various geographical locations of Iran.

**Results:** The average annual number of human cases of CE was 274.8. Among 31 provinces of Iran, Razavi Khorasan from northeast part of Iran was the highest human CE infected province with the 1801 cases and Hormozgan Province in south part of the country showed the lowest the disease with the only one case of CE in 2009. Liver and lungs with the infection rate of 61% and 20%, respectively are the most infected organs, 53% of patients had one cyst in the bodies and the number of cysts in 8% of cases was more than 3 cysts. Altogether, 41% of CE cases were treated by surgery, 11% with chemotherapy and 48 % with mixed surgery and chemotherapy.

**Conclusion:** Human CE is a major health problem in Iran and it is necessary to establish basic control programs. It is crucial to setting up standard diagnostic methods for early diagnosis, effective treatment, plan educational schedule for different social levels and control the disease in both definitive and intermediate hosts.

**Keywords:** Cystic echinococcosis, Human, Iran

### Introduction

Human cystic echinococcosis or human hydatidosis is a zoonotic infection caused by larval forms (metacestodes) of tapeworms of the genus *Echinococcus* spp. live in the small intestine of domestic and wild canines. Although there are different species of *Echinococcus* described, only two of them including *E. granulosus* and *E. multilocularis* are pathogenic for humans. To differentiation the diseases caused by these two different species, WHO proposed the designation Cystic Echinococcosis (CE) for the disease caused by *E. granulosus* and Alveolar Echinococ-

cosis (AE) for the disease caused by *E. multilocularis* (1).

Human echinococcosis is a zoonotic parasitic infection caused by the larval stage of *E. granulosus* recommended to be appointed in neglected parasitic disease by WHO reports (1). Echinococcosis is a main public health concern, especially in developing countries with inadequate economic resources (1-4). Human hydatidosis is commonly asymptomatic and endurable for many times until they cause a force on neighboring tissues. They have usually diagnosed acci-

dentially during exploration for other pathology(5). The clinical manifestations are similar to a slowly growing tumor and depend on the size, number and the site of the cyst(6). About 60%-70% of CE takes place in the liver and 20%-25% in the lungs. Bones, kidneys, spleen, muscles, CNS and behind the eye are the other organs infected by cysts(7). Dogs and other canines are the definitive hosts for *E. granulosus* that subclinically carry the adult form of the worm and because of the close relationships to humans are particularly important in zoonotic transmission(8). Humans, sheep, cattle, buffalo, camels, and pigs are the commonest intermediate hosts that infected by the ingest tapeworm eggs from foods and contaminated water (9). Hydatid disease is particularly common in rural regions, chiefly sheep-raising areas. The annual incidence of human CE can range from less than 1 to 200 per 100000 inhabitants in various endemic areas (10). CE is endemic in the entire Mediterranean regions including all countries from the Middle East. Hydatidosis is endemic in Iran so it must be considered as a problem. Five to 49% of stray dogs are infected with *E. granulosus* in different areas of Iran. Sheep, camels, and cattle with the prevalence rate of 88%, 70% and 10%, respectively are the main intermediate host in Iran (11). In the present study, we estimated the pattern of human CE in the Iran from 1995 to 2014.

## Methods

This retrospective study was designed using data from the national hydatidosis surveillance system. The communicable diseases control organization of the Iranian Ministry of Health is responsible for surveillance and passive collection of data of communicable diseases from various provinces of Iran. Computerized Tomography (CT) scans serology; echography and sonographic methods are mostly using in diagnosis of human CE in this study (12). Hydatidosis surveillance data from different governmental and private hospitals in all parts of country, were should record in Health Information Management. These data monthly submitted to the communicable diseases

control organization of the Iranian Ministry of Health. In current work, data from 1995 to 2014 monthly gathered online from 355 districts. The data collected for this survey included individual and geographical information, laboratory data and treatment methods for all cases of human CE. The zoonosis department is a subset of the communicable diseases control organization and similar information for human CE was assessed and analyzed by this department.

Ethical approval for the study was obtained from the national hydatidosis expert committee.

The data were analyzed using SPSS software (Chicago, IL, USA, version 19.0), and Microsoft Excel 2010 at the communicable diseases control organization.

## Results

### *Trends of incidence rate of human CE during 1995-2014:*

The data on all types of echinococcosis in Iran were collected from 1995 to 2014. Over this period, the total number of cases reached 8518. The trend in cases of human CE from 1995 to 2014 is illustrated in Fig. 1, showing the number of the cases in each year. The highest incidence rate of echinococcosis was reported in 2010 with 615 cases and the lowest in 2007 with 246 cases.

Among 31 provinces of Iran, Razavi Khorasan Province from northeast was the more infected province with the 1801 CE cases and the lowest rate of CE was reported from Hormozgan Province in the south part of the country with the only one case in 2009 (Fig. 2).

Table 1 shows the distribution of human CE in various geographical zones of Iran reported during 1995 – 2014.

### *Epidemiological profile of CE in 2014*

Fig. 3 illustrates the distribution of human CE in each province of the country in 2014. In that year, 550 cases were recorded. Razavi Khorasan, Tehran and Isfahan provinces had the highest incidence rates at 91, 58 and 48 cases, respectively.

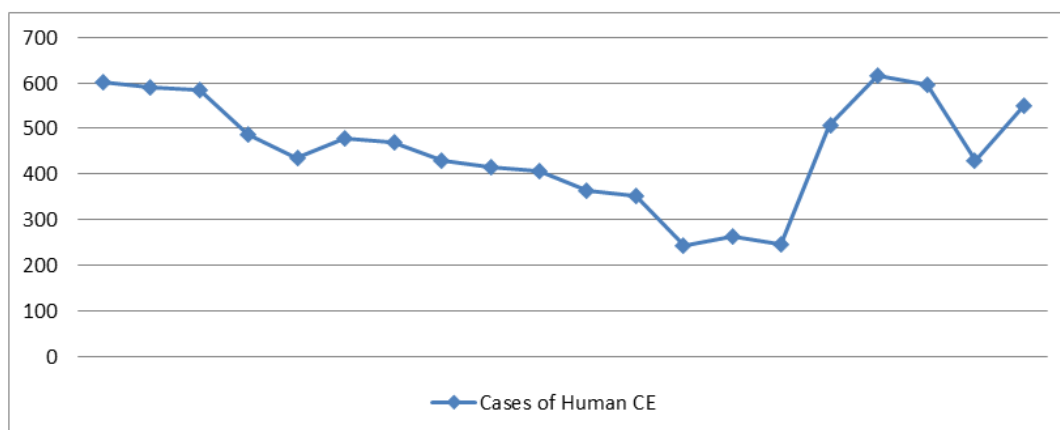


Fig. 1: Trend of human CE in Iran, showing number of cases and incidence rate per 100 000 inhabitants, 1995–2014

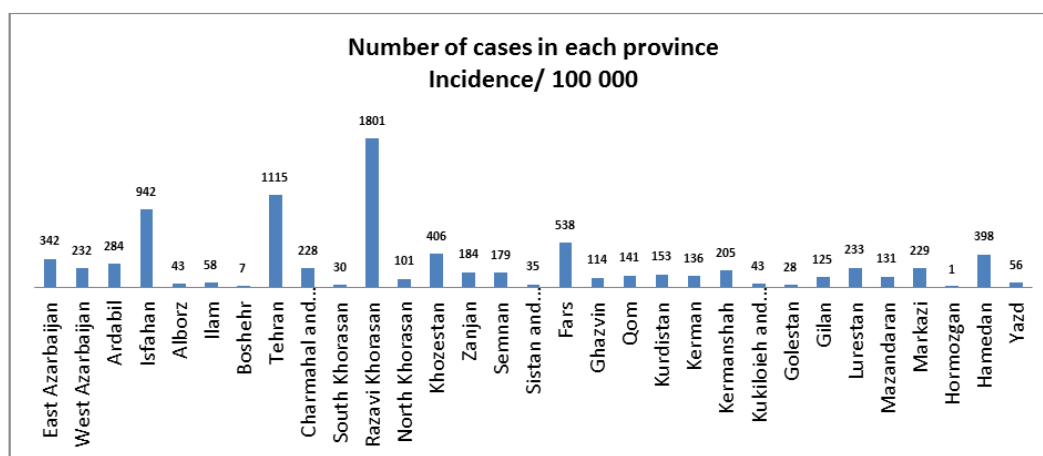


Fig. 2: Incidence rate of human CE in different provinces of Iran during 1995- 2014

Table 1: Distribution of human CE in different areas (North, East, West, South and Center) of Iran during 1995-2014

Geographical locations	1995																			
	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
North	13	18	18	17	23	13	25	20	8	6	16	24	16	19	17	27	25	23	32	38
East	46	49	84	62	10	12	13	75	10	17	12	10	68	93	79	10	81	10	82	97
West	37	47	87	63	67	69	56	39	48	56	39	56	55	33	36	79	115	117	98	107
South	61	60	63	83	28	29	20	10	12	20	16	9	9	5	9	9	10	8	4	10
Center	44	41	33	27	21	25	23	29	24	15	17	16	99	11	10	28	40	35	28	30
Total	5	1	6	5	6	1	8	1	6	8	1	7		5	6	3	3	6	6	6
Total	602	590	584	486	435	478	470	429	414	406	364	352	242	263	246	506	615	596	429	550

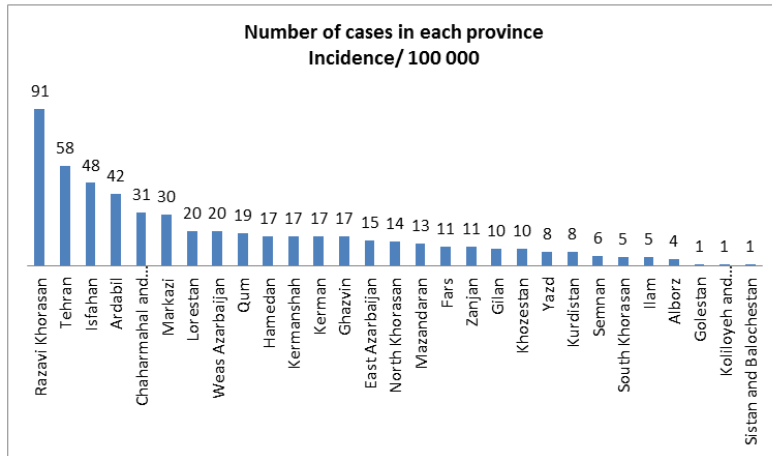


Fig. 3: Incidence rate of human CE in different provinces of Iran in 2014

According to, the highest annual incidence of new human CE in 2014 occurred in Mar, with 59 cases (10.72%), while the lowest rate was reported in Sep, with 37 cases (6.72%) (Fig. 4). Figures

5 and 6 show the distribution of human CE total cases and new cases of human CE in various parts of Iran.

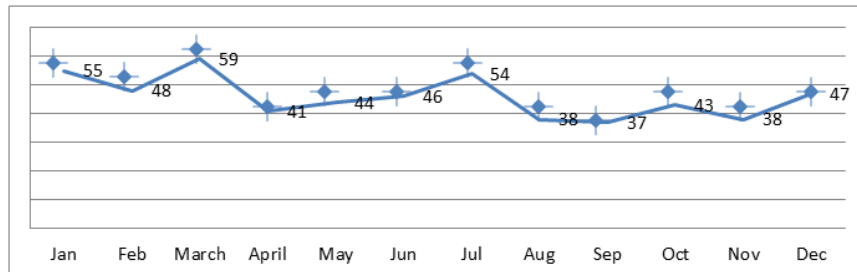


Fig. 4: Number of cases of Hydatidosis in different months in 2014, Iran

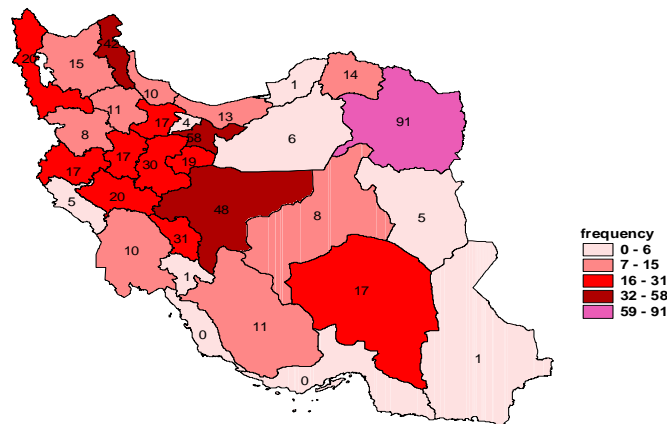
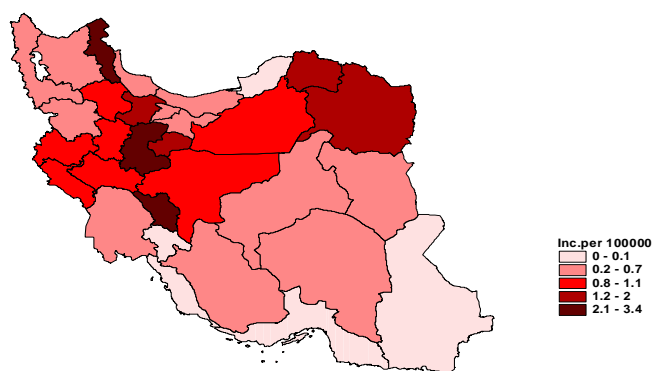


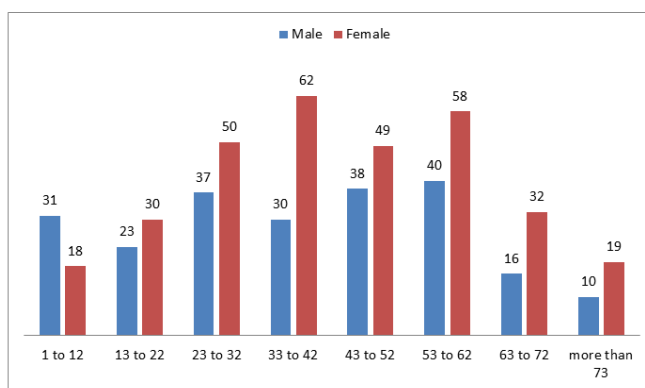
Fig. 5: Distribution of human CE in different provinces of Iran, 2014



**Fig. 6:** Distribution of Incidence of human CE in different provinces of Iran per 100000 inhabitants

Overall, 57%, 42% and 1% of patients were reported from Rural, urban and nomads' areas, respectively. In current work, 60% of the vegetable were washed only by water. Detergents were used

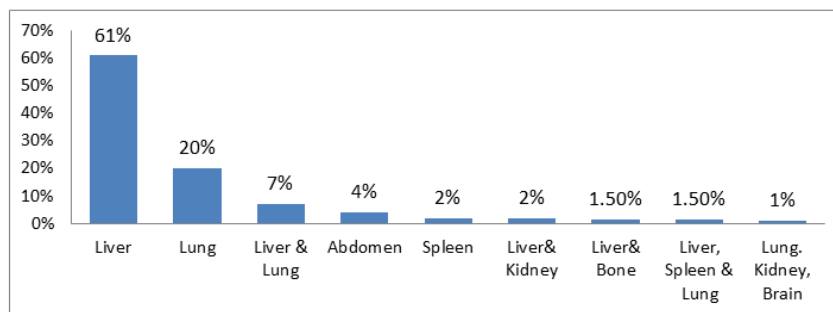
in 28% and disinfectants were used in 5% and 7% of vegetables were washed by all of them. Fig. 7 shows the distribution human CE among various age groups in all parts of Iran.



**Fig. 7:** Distribution of human CE among different ages in Iran, 2014

Liver, and lungs with the infection rate of 61% and 20%, respectively were the most involved organs (Fig. 8). Fifty-three percent of our cases had one cyst in their body. Two cysts and 3 cysts

forming 18% and 7% of cases, respectively. In 8% of cases, number of cysts was more than 3 cysts and in 14% the number of cysts was unknown.



**Fig. 8:** Distribution of human CE in different organs of patients in Iran, 2014

Three treatment options were used in our cases: surgery (in 41% of cases), drug treatment or chemotherapy (in 11% of cases) and mixed method (in 48% of cases). In this study, 52% of patients had no contact with dog and 48% have contact; of course, this difference was not statically significant. From all patients, 21 and 1 cases were from Afghanistan and Iraq, respectively.

## Discussion

WHO enumerates hydatidosis as one of the most serious global concern and has encouraged to focus on its prevention and control (13-15). However, due to the complex epidemiological aspects with various hosts and asymptomatic diseases, investigation, and control of the disease are very difficult. Human CE continues to be a significant public health problem in numerous countries. From several regions, there are alarming indications of increasing human health risks caused by echinococcosis(16).

*E. granulosus* has a global distribution and happens in all circumpolar, temperate, subtropical and tropical zones (17, 18). The prevalence of the parasite varies from sporadic to high and parts of Europe, Asia, Africa, Australia and South America have highest prevalence of *E. granulosus* (Fig. 4).

Current work indicated the trend in hydatidosis incidence in Iran from 1995 to 2014 and focused on the epidemiological position in 2014. We recorded an annual average of 8518 cases of hydatidosis over the two decades of the study and an annual average incidence of 18.96 per 100000 inhabitants. In Europe, northern and central areas have very low prevalence rates, regions of southern, south-eastern and eastern regions have medium or high prevalence rates and Iceland and Greenland are free of the parasite (18, 19). The annual incidence rates of human cases of cystic echinococcosis (CE) in some European countries varied between <1.0 and >8.0 per 100000 population. In Republic of China, the average annual incidence was 8.7 per 100000 in 1990(20).

The Ministry of Health of Turkey during 1987 and 1994 has recorded 21303 human cases of CE, with an annual incidence rate is 4.4 per

100000 inhabitants (21). In Our Northern neighbor, in Russia, during 15 yr (1983-1997) a total of 2863 cases of human Cystic echinococcosis was officially recorded (average of 191 cases per year) (22). 2.87% of Yemen human population was infected by Cystic echinococcosis(23). In 2014, 550 cases were recorded and Razavi Khorasan Province had the highest incidence rates at 91cases(24). Razavi Khorasan Province is neighbor with Pakistan and infected animal and foods may transfer the infection. In a study in Hyderabad, Pakistan recorded that 44 cases out of 43656 registered patients were polluted with cystic echinococcosis (25).

The highest morbidity rate of human CE was reported among 6 -20 years ages (3, 26). (3, 26). The most commonly affected age group in our survey was 33– 42 yr, followed by 53–62 yr. In New Zealand, patients with 25- 44 yr of old were more infected with human cystic echinococcosis (22). Similarly, in Tasmania, 45- 54 yr patients were more polluted (15, 27). Unlike to our study, the age group of less than 20 yr old higher rates of infection (5.0%); and the age group of 41-60 yr old have lower rate (1.33%) in Yemen (23). In another study in Uruguay, the age groups between 70 to 79 yr were most polluted than other age groups (28).

According to our results, human CE also affected slightly more females than males in most of age groups; but the difference was not statically significant. In a study in Yazd Province, 50% of the infected individuals were female and 50% were male (29). Similar to current work, in most series of individuals, their differences in the gender ratios of patients with CE were no significant (12, 26, 30). Of course, in a survey in Yemen all patients were female (23). The high infection rate in woman is probably due to more contact with dogs and because of the dogs being intense around the household where women spend most of their times.

According to geographical areas, because of the closer contact with dogs and low quality of education and health information, rural areas are usually more polluted than urban areas. CE happens most regularly in rural areas (31, 32). Over-

all, 57% of patients were from rural areas, 1% was from nomads and others were from urban areas. The prevalence/incidence in urban areas is higher in compared to rural areas (33).

Liver and lung were the most ordinarily affected organs. Most of human cysts are clinically silent and are diagnosed accidentally or when complications befall (34). A study in Yazd Province showed that 75% of human hydatid cyst to be held in Liver (29). Reports indicate very rare incidence of the disease in other sites such as the heart, spleen, pancreas, and muscles (22). In our work, 4% and 2% of cysts formed in abdomen and spleen, respectively. The splenic contribution in hydatid disease is infrequent, routinely less than 2%-6% of all human *Echinococcus* cases. The infestation of the spleen commonly follows by two ways: 1: by arterial route through the hepatic and pulmonary filters, 2: rearward venous route (35, 36).

There are now three treatment choices for hydatid disease: surgery, which remains the most efficient treatment (37). Chemotherapy (secondary) is preferred where surgery is not accessible or when there are numerous cysts, and in unfeasible cases (38). In 3rd method, chemical drugs have also been used as an addition to surgery for prevention of spillage of cyst insides (39, 40). Because of the passive surveillance of data collection, some defects and limitations in data collection and report may happen.

## Conclusion

Human CE is still a major problem for health system of Iran and need to establish basic control programs. It is crucial to setting up standard diagnostic methods for early diagnosis, effective treatment, plan educational schedule for different social levels and control the diseases in different definitive and intermediate hosts.

## Ethical considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or fal-

sification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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## Conflict of Interest

The authors declare that there is no conflict of interests.

## References

1. Wilson JF, Rausch RL, McMahon BJ, Schantz PM (1992). Parasitocidal effect of chemotherapy in alveolar hydatid disease: review of experience with mebendazole and albendazole in Alaskan Eskimos. *Clin Infect Dis*, 15(2): 234-49.
2. Schantz PM, Van den Bossche H, Eckert J (1982). Chemotherapy for larval echinococcosis in animals and humans: report of a workshop. *Z Parasitenkd*, 67(1): 5-26.
3. Ammann RW, Eckert J (1996). Cestodes: *Echinococcus*. *Gastroenterol Clin North Am*, 25(3):655-89.
4. Bresson-Hadni S, Vuitton DA, Bartholomot B et al (2000). A twenty-year history of alveolar echinococcosis: analysis of a series of 117 patients from eastern France. *Eur J Gastroenterol Hepatol*, 12(3):327-36.
5. Budke CM, Carabin H, Ndimubanzi PC et al (2013). A systematic review of the literature on cystic echinococcosis frequency worldwide and its associated clinical manifestations. *Am J Trop Med Hyg*, 88(6): 1011-1027.
6. Nunnari G, Pinzone MR, Gruttadauria S et al (2012). Hepatic echinococcosis: clinical and therapeutic aspects. *World J Gastroenterol*, 18(13):1448-58.

7. Kvascevicus R, Lapteva O, Awar AO et al (2016). Fatal Liver and Lung Alveolar Echinococcosis with Newly Developed Neurologic Symptoms due to the Brain Involvement. *Surg J (N Y)*, 2(3):e83-e88.
8. Wassermann M, Aschenborn O, Aschenborn J et al (2014). A sylvatic lifecycle of *Echinococcus equinus* in the Etosha National Park, Namibia. *Int J Parasitol Parasites Wildl*, 4(1):97-103.
9. *Encyclopedia of Parasitology*, Mehlhorn H, 4<sup>th</sup> edition, Springer, Heidelberg, New York, (2015).
10. Zhang W, Zhang Z, Wu W et al (2015). Epidemiology and control of echinococcosis in central Asia, with particular reference to the People's Republic of China. *Acta Trop*, 141:235-43.
11. Rokni MB (2009). Echinococcosis/hydatidosis in Iran. *Iran J Parasitol*, 4(2):1-16.
12. Cohen H, Paolillo E, Bonifacino R et al (1998). Human cystic echinococcosis in a Uruguayan community: a sonographic, serologic, and epidemiologic study. *Am J Trop Med Hyg*, 59(4): 620-7.
13. World Health Organization (2013). *Sustaining the drive to overcome the global impact of neglected tropical diseases: second WHO report on neglected tropical diseases*.
14. 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 Med*, 12(12):e1001920.
15. Torgerson PR, Budke CM (2003). Echinococcosis—an international public health challenge. *Res Vet Sci*, 74(3):191-202.
16. Possenti A, Manzano-Román R, Sánchez-Ovejero C et al (2016). Potential Risk Factors Associated with Human Cystic Echinococcosis: Systematic Review and Meta-analysis. *PLoS Negl Trop Dis*, 10(11):e0005114.
17. McManus DP, Zhang W, Li J, Bartley PB (2003). Echinococcosis. *Lancet*, 362(9392): 1295-304.
18. Budke CM, Deplazes P, Torgerson PR (2006). Global socioeconomic impact of cystic echinococcosis. *Emerg Infect Dis*, 12(2):296-303.
19. Skírnisson K, Richter SH, Eydal M (2003). Prevalence of human parasites in Iceland: past and present status. *Parasites of the Colder Climates Taylor & Francis, London and New York*, 23(1): 34-44.
20. Chi P, Zhang W, Zhang Z et al (1990). Cystic echinococcosis in the Xinjiang/Uyghur Autonomous Region, People's Republic of China. I. Demographic and epidemiologic data. *Trop Med Parasitol*, 41(2):157-62.
21. Altintas N (2003). Past to present: echinococcosis in Turkey. *Acta trop*, 85(2):105-12.
22. WHO/OIE manual on Echinococcosis in Humans and animals : Geographic distribution and prevalence / edited by Eckert J, Schantz P, Gasser R, Torgerson P, Bessonov A, Movsessian S. 2001, 13(5): 100-142.
23. Al-Shaibani I, Saad FA, Al-Mahdi H (2015). Cystic echinococcosis in humans and animals at Dhamar and Taiz governorates, Yemen. *Int J Current Microbiol Appl Sci*, 4(1):596-609.
24. Beiromvand M, Akhlaghi L, Massom SHF et al (2011). Detection of Echinococcus multilocularis in carnivores in Razavi Khorasan province, Iran using mitochondrial DNA. *PLoS Negl Trop Dis*, 5(11): e1379.
25. Latif AA, Tanveer A, Maqbool A et al (2010). Morphological and molecular characterisation of Echinococcus granulosus in livestock and humans in Punjab, Pakistan. *Vet Parasitol*, 170(1-2):44-9.
26. WHO/OIE manual on echinococcosis in humans and animals : a public health problem of global concern / edited by Eckert, J, Gemmell, M. A, Meslin, François-Xavier, Pawlowski, Z. S. 2001,90-265.
27. Thompson RC, McManus DP (2002). Towards a taxonomic revision of the genus Echinococcus. *Trends Parasitol*, 18(10):452-7.
28. Perdomo R, Alvarez C, Monti J et al (1997). Principles of the surgical approach in human liver cystic echinococcosis. *Acta Trop*, 64(1-2):109-22.
29. Ali Fattahi Bafghi, Mahin Ghafourzadeh (2015). Pattern of Human Hydatid Cyst in the Province of Yazd, Iran (2006-2011). *Int J Med Lab*, 2(2):128- 33.
30. Pearson M, Le TH, Zhang L, Blair D, Dai THN, McManus D (2002). Molecular taxonomy and strain analysis in. Cestode Zoonoses: Echinococcosis and Cysticercosis—*An Emergent and Global Problem*, IOS Press, Amsterdam, 205-19.
31. Macpherson C, Spoerry A, Zeyhle E, Romig T, Gorfe M (1989). Pastoralists and hydatid disease: an ultrasound scanning prevalence sur-



- vey in East Africa. *Trans R Soc Trop Med Hyg*, 83(2):243-7.
32. Craig PS, Rogan MT, Allan JC (1996). Detection, screening and community epidemiology of taeniid cestode zoonoses: cystic echinococcosis, alveolar echinococcosis and neurocysticercosis. *Adv Parasitol*, 38:169-250.
  33. Mihăilă DE, Potecă TD, Potecă A, Pițuru S (2015). Single-center epidemiological study on the incidence of hepatic hydatid cyst. *Rom J Intern Med*, 53(2):170-3.
  34. Shapiro SZ, Bahr GM, Hira PR (1992). Analysis of host components in hydatid cyst fluid and immunoblot diagnosis of human *Echinococcus granulosus* infection. *Ann Trop Med Parasitol*, 86(5):503-9.
  35. Safioleas M, Misiakos E, Manti C (1997). Surgical treatment for splenic hydatidosis. *World J Surg*, 21(4):374-8.
  36. Malik AA, ul Bari S, Younis M, Wani KA, Rather AA (2011). Primary splenic hydatidosis. *Indian J Gastroenterol*, 30(4):175-7.
  37. Adas G, Karatepe O, Altıok M et al (2009). Diagnostic problems with parasitic and non-parasitic splenic cysts. *BMC Surg*, 9(1):1-7.
  38. Wen H, New RR, Craig PS (1993). Diagnosis and treatment of human hydatidosis. *Br J Clin Pharmacol*, 35(6):565-74.
  39. Blanton RE, Wachira TM, Zeyhle EE et al (1998). Oxfendazole treatment for cystic hydatid disease in naturally infected animals. *Antimicrob Agents Chemother*, 42(3):601-5.
  40. Spicher M, Roethlisberger C, Lany C et al (2008). In vitro and in vivo treatments of *Echinococcus* protoscoleces and metacestodes with artemisinin and artemisinin derivatives. *Antimicrob Agents Chemother*, 52(9):3447-50.