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Review Article

Echinococcosis /hydatidosis in Iran

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Abstract

Cystic echinococcosis caused by *Echinococcus* spp. is considered endemic in Iran. To clarify the present status of hydatidosis in Iran the present review article is presented. Authentic databases and search engines from 1996 onwards were utilized to enquire the situation of the disease in Iran. Human hydatidosis is responsible for approximately 1% of admission to surgical wards and the rate of human infection is 0.6-1.2/100000. The usual order of involvement, i.e. liver, lung, and other organs, respectively is documented here as well. Risk factors include contact with dog, eating vegetable, geophagy and contact with sheep. Dogs play a critical role in transition the hydatidosis. The rate of infection with *E. granulosus* in stray dogs shows a prevalence of 5% to 49% in different parts of Iran. Followed by sheep with 88% fertilized cysts, camel with 70%, and cattle with 19% have been considered as the most important and the weakest intermediate host of *E. granulosus*, respectively. Molecular analyses clearly indicate that the camel/dog strain (G6 genotype) of *E. granulosus* as well as the cosmopolitan, common sheep strain (G1 genotype) occurs in Iran. A wide variety of livestock including sheep, cattle, goat, camel and buffalo also harbor the disease. *E. multilocularis* another agent of human hydatidosis (alveolar cyst) is reported here as well and from 1946 to 1993, 37 cases of human alveolar echinococcosis were reported from northwestern Iran. Hydatidosis must be considered as a dilemma in Iran because of its endemicity in the country.

Keywords: *Cystic, Alveolar, Echinococcosis, Hydatidosis, Animal, Human, Iran*

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Introduction

Hydatisidosis, caused by *Echinococcus* spp. (*E. granulosus* and *E. multilocularis* in Iran) is one of the most important zoonotic diseases, throughout the most parts of the world. Ingesting embryonated eggs through hands, food, drinks or material contaminated with parasite eggs infects humans; the larvae reach the blood and lymphatic circulation and transport to the liver, lungs and other organs (1). The asymptomatic period is too long and the disease might be diagnosed even after 20-25 years post infection.

Cystic echinococcosis is considered endemic in the entire Mediterranean zone including all countries from the Middle East, but alveolar echinococcosis is less prevalent and has been reported only from Iran, Turkey, Iraq and Tunisia(2). Hydatidosis is endemic in Iran and is responsible for approximately 1% of admission to surgical wards (3-5). In the recent years, there has not been a documented review article to show the trend of hydatidosis in Iran. Hence, the present review article aims to have a glimpse at the present status of echinococcosis/hydatidosis in Iran.

Search approach

Databases and search engines of EMBASE, ISI web of Science, PUBMED, SCIRUS, IRAN MEDEX, GOOGLE SCHOLAR, and CABI were utilized. Published bibliographies not inserted in Internet were manually searched. For more accuracy, documents of not peer reviewed approval such as undocumented hospital records or proceedings of the congresses were not included in the scheme but a few cases. Database searches were restricted mostly from 1996 to 2008. In occasional cases, to compare the previous and present situation some data were included originated before aforementioned

date. It is worth mentioning that *E. granulosus* and *E. multilocularis* are not reportable diseases in Iran. The panel of key words was as follows:

“helminthiasis”, “helminths”, “cestodes”, “Prevalence”, “*Echinococcus multilocularis*”, “*Echinococcus granulosus*”, “hydatidosis”, “cystic echinococcosis”, “alveolar echinococcosis”, “hydatid disease combined with “Iran” at the beginning.

Echinococcus granulosus

E. granulosus is the causative agent of cystic hydatid disease or hydatidosis, whereas infection with *E. multilocularis* in man leads to the more aggressive form of alveolar echinococcosis.

Different strains in Iran

In a study conducted on 16 isolates of *E. granulosus* from domestic animals including sheep, goats, cattle, and camels, DNA nucleotide and predicted amino acid sequence variation within regions of the mitochondrial cytochrome oxidase I (COI) and NADH dehydrogenase subunit I (NDI) genes were analyzed (6). It was indicated that the camel/dog strain (G6 genotype) of *E. granulosus* as well as the cosmopolitan, common sheep strain (G1 genotype) occurs in Iran. The G1 genotype was present in all four human isolates examined. They reported G1 genotype for livestock including sheep, cattle and goat in different parts on Iran. Besides, they reported G6 genotype for camels in central Iran. The authors concluded that in *E. granulosus* endemic areas of Iran the majority of *E. granulosus* infected livestock animals could potentially act as reservoirs of human infection, and this had important implications for hydatid control and public health(6).

In another report, the sheep strain was the most common genotype of *E. granulosus* and the majority of camels were infected with the camel genotype, besides three of 33 human cases (7).

Prevalence of human hydatidosis based on the hospital reports in different parts of Iran

Table 1 shows the frequency of hydatidosis in different parts of the country (Fig. 1), framed on a retrospective study and collecting data using study of patients' cases after surgery, i.e. hospital based. These data embrace the reality that the disease is not confined to a special part but throughout the country. Khorasan Province embraces the most cases consequently and this has been acknowledged via other studies. Interestingly in Hamadan Province (west of Iran) it is obvious that from 1982-1992 (10 yr) totally 55 cases have been reported while from 1999-2006 (7 yr), 179 cases were reported. We have no idea if the rate of infection is increasing in this region or the improvement of facilities caused patients to go under surgery in their area. A comprehensive study in Iran shows the overall prevalence as 2083 cases from 2001-2005 (8).

Organ involvement

As it is expected from the parasite circulation in the body, nearly most of the studies conducted here witness the involvement of the liver at the highest degree, e.g. 90.5% (23), 69.23% (19), 61.5% (22) and 71.6% (12). In few studies lung has the majority of involvement, e.g. 44.8% vs. 39.4% of liver involvement (14). Of course, the authors confirmed that this was an unusual consequence and might be due to having more facility of treating lung diseases in the region.

Table 2 presents some cases of organ involvement except than liver and lung.

Nearly all parts of the body have a record in the literature found here. A detailed report from Mashhad of 1759 human hydatidosis cases shows involvement of orbit, lymphatic glands, tonsil, pancreas, skin, ovary, uterus and parotid glands (14).

Seroprevalence of human hydatidosis in different regions of Iran

Table 3 confers data collected using different screening tests stated in the table. A rate of 1.2-21.4% of infectivity is obvious in different parts of the country. Evidently, the rate of 21.4% in Chahar Mahal va Bakhtyari Province can not be trusted because the method of estimation was Casoni test which is not reliable especially for positive responses. The problem is that Tehran is the capital and many people of different races live there so it is obviously difficult to decide on the originality of infected people.

Incidence

Unfortunately, during the recent years it is not easy to find a comprehensive study in terms of incidence. The annual incidence rate of hydatidosis in human in Hamadan as 1.33 cases/100,000 (23), in Kashan 3/100,000 populations (15), in Babol 1.18/100,000 (11), and throughout Iran 0.61/100,000 (47) are among documented reports.

Age distribution

According to Table 1, and in coincidence with global evidence, hydatidosis in Iran has no privilege for age. Hydatidosis is a disease of long incubation period (might be 20 to 30 yr) and accordingly a wide range of different ages is obvious in infected patients. The overall deduction shows the range of 20-40 years old as the age group of the highest cases.

Sex distribution

Looking at Table 1 shifts the balance of infection rate to females (References in the table). Women have the highest chance of contact with sources of infection such as dog, soil, vegetable etc, yet in some areas depending on the culture and social criteria it is possible that men cover the highest rate of infection. The next paragraph holds out more details.

Occupation distribution

Nearly in all stated references in this paper, conducted in Iran, the housewives encompass the highest rate of infection (51.3% - 75%). Housewives, especially in rural areas, where the most infected cases can be found, have the highest chance of contact with the sources of infection. Contact with contaminated vegetables, cleaning the house containing the dog faeces, desire to eat soil (Geophagy) as longing in pregnant embrace the etiological issues.

Laboratory diagnosis of hydatidosis in Iran

Not mention of routine methods such as CT-scan, MRI, X-ray and so on, in Iran, many serological methods have been evaluated to diagnose hydatidosis so far. ELISA and Fast-ELISA with sensitivity, specificity, positive and negative predictive values of 96.7%, 95.2%, 93.7%, 97.5%, and 100%, 97.5%, 96.7%, 100%, respectively have been evaluated here (48). Dot-ELISA (49), (5), Enzyme-linked Immuno-electro Transfer Blot (EITB) (50), ELISA (51) are only some methods reported here to diagnose hydatidosis. At present, ELISA method using AgB is the most efficient test and is accessible in some laboratories (52). The challenge is to diagnose the acute cases and following the patients after treatment. Up to date, no authentic laboratory method has been established here to hold this role.

Risk Factors

Vegetable: Here is tendency to eat raw vegetables with food. Unfortunately, in most vegetable farms, dogs freely prowl and contaminate the vegetables. Another potential source of infection is carrot juice, which almost everywhere is sold in a mixture with ice cream. The washing system of carrots is such that the parasites' eggs are retained in washing water and most of them are not separated from the carrots (53).

Geophagy: A tendency to eat soil by pregnant women especially in rural areas makes the situation in benefit of infecting with hydatidosis. The author encountered with a female infected with severe hydatidosis who had the habit to eat soil with spoon and her husband had to close her hands when he was going to work. Children also play a game (local name: Tileh bazi) entails them to contact with soil. A rate of 70% geophagy was reported in hydatidosis cases (54). In another study from 670 soil samples collected from 135 villages in various parts of Iran, 10.3% contained taeniid eggs (55). It is worth mentioning that the eggs of *Echinococcus* and *Taenia* spp. are morphologically indistinguishable (56).

Sheep: Vicinity of sheep with dogs in places selling sheep results to contamination of sheep wool with parasite's eggs. Sheep sellers contact them and while counting money, eating or drinking, ingest the eggs. Shepherds also can be infected in this manner. Sixteen cases of hydatidosis (52%) had a history of contact with dogs or sheep (17). Sheep shearing as a routine task in rural areas especially nomads is another risk factor.

Other risk factors

Contacting with dog (will be discussed later) and breast pumping are two other great risk factors here.

Transmission cycles in Iran

So far three distinct cycles of *E. granulosus* have been suggested: A domestic cycle between dogs and livestock, a desert cycle between dogs and camels and a sylvatic cycle between wild carnivores and wild ruminants. In domestic cycle, the mean prevalence of *E. granulosus* in domestic dogs is 23.45%, which vary widely from 3.3 to 63.3% depending on the local condition (57).

In Iran followed by sheep (with 88% of fertilized cysts), camel (having 70% of fertilized cysts), and cattle (with 19% fertilized cysts) have been considered as the most important and the weakest intermediate host of *E. granulosus* (58).

Animal studies

Dog

Dogs play a critical role in transition the hydatidosis. Dog registration is not enforced in Iran. Survey of literature regarding the rate of infection to *E. granulosus* in stray dogs shows a prevalence of 5-49% in different parts of Iran (59- 61). The number of sheepdogs can be roughly estimated at 700,000 in Iran; hence, a large number of parasites' eggs may be released each day in the region (57). Dogs infected with *E. granulosus* freely go to vegetable fields and infect them. Here is tendency to eat raw vegetables with food. Survey of literature regarding the rate of infection to *E. granulosus* in stray dogs is represented in Table 4. In a widespread study conducted in 13 provinces of Iran, the prevalence of *E. granulosus* in sheepdogs was detected as 27.17% (57). Accordingly, the lowest and the highest prevalence was 3.3% and 63.3% in Sistan & Baluchestan and Esfahan, respectively.

Intensity of infection with *E. granulosus* in dogs was reported as 3-2000/dog in western Iran (61). Regarding worm burden in dogs, in a study, 81% of infected dogs had

1-100 worms, 13% had 100-1000 and 4% had >1000 worm burdens (62). In another study, most dogs harbored fewer than 50 worms (57).

Hydatidosis in livestock

The prevalence of infection with hydatid cyst in sheep, goats, cattle and buffaloes in various regions of Iran is exposed in Table 5. All these data have been gathered using abattoir inspection and records. The highest and the lowest rate of infection were in Ardabil and Qom provinces, respectively. Accordingly, all these animals having the label of intermediate hosts can be regarded as the source of infection. In a comprehensive new study, the average of infection in livestock reported 6.73% (47). As a result, the highest and the lowest rate of infection were in Khorasan and Yazd, respectively. Religious ceremonies in Muslim countries entail the sacrifice of livestock, which have the risk of spreading the disease, but the public health authorities have established a monitoring system to decrease the risk of infection.

Camel

A five-province based study was conducted, in which 35.2% (233/661) of slaughtered camels were infected with hydatidosis (81). The degree of prevalence between males (34.4%) and females (36.6%) was not statistically significant. The highest rate of infection (59.3%) was found in Isfahan Province (central Iran) while the lowest (25.7%) was found in Kerman Province. The organ distribution of cysts was 49.4% in lungs alone, 30.0% in both liver and lungs, 14.6% in liver only and 6.0% in other organs. The fertility rate of lung cysts (69.7%) was higher than that of liver cysts (58.7%) and other organs (50.0%). In another study, the characteristics of larval and adult isolates of *E. granulosus* from sheep and cattle, although

similar, showed significant differences from those of the camel isolates, especially with respect to the size of rostellar hooks (58). In dogs experimentally infected with the three 'strains' of *E. granulosus*, the rate of development was more rapid in the camel than two others were. In addition, adult camel originated *E. granulosus* demonstrated differences in worm length, segmentation and size, shape, number and arrangement of the genitalia when compared with worms derived from sheep and cattle (58). On epidemiological grounds, camels appear to be an important reservoir for human infection (82).

Carnivorous

A study on various carnivores from Hamadan, Azarbaijan and Tehran provinces using coproantigens -ELISA showed the prevalence of *Echinococcus* spp. infection as 43.1 % (83). Studies in five provinces in western Iran on 86 golden jackal, 60 red foxes and 3 female wolves (*Canis lupus*) showed the infection of 2.3% of the golden jackals and 5% of the red foxes to *E. granulosus* (61).

E. multilocularis

E. multilocularis is another agent of human hydatidosis (alveolar echinococcosis) with red fox (*Vulpes vulgaris*) and jackal (*Canis aureas*) as final hosts as well as social vole (*Microtus socialis*) as intermediate host (84) in Iran , where is recognized an endemic country for the disease (82). From 1946 to 1993, thirty seven cases of human alveolar echinococcosis were reported in Azerbaijan Province, northwestern Iran, form that, 76.9% were female (85). Age group of 31-45 yr old took in the highest rate and 38.2% of cases were farmers, followed by shepherds 32.6%, workers 11.1% and another jobs such as hunters and housewives 17%. Liver and lung had the rate of infection as 92.3% and 7.6%, respectively.

The first animal report of *E. multilocularis* in Iran was that of Mobedi et al. in 1971 where 10% of examined red foxes showed infection with this parasite (84). Moreover, 22.9% of red foxes and 16% of jackals demonstrated infection with the parasite in Ardabil Paovince (85).

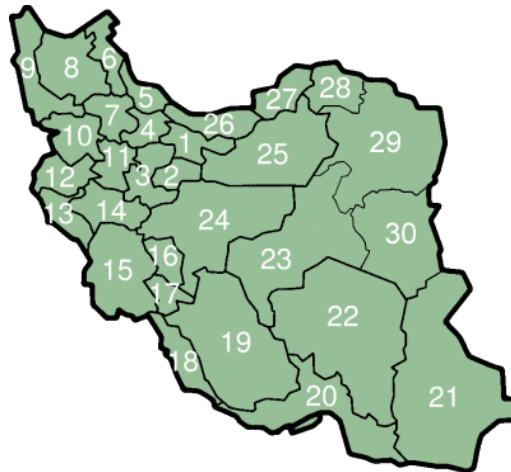


Fig. 1 : Iran consists of 30 provinces as follows:

- 1- Tehran, 2- Qom, 3- Markazi, 4- Qazvin, 5- Gilan, 6- Ardabil, 7- Zanjan, 8- East Azarbaijan, 9- West Azarbaijan, 10- Kurdistan, 11- Hamadan, 12- Kermanshah, 13- Ilam, 14- Lorestan, 15- Khuzestan, 16- Chahar Mahal and Bakhtyary, 17- Kohkiluyeh and Boyer Ahmad, 18- Bushehr, 19- FArS, 20- Hormozgan, 21- Sistan and Baluchistan, 22- Kerman, 23- Yazd, 24- Esfahan, 25- Semnan, 26- Mazandaran, 27- Golestan, 28- North Khorasamn, 29- Khorasan Razavi, 30- South Khorasan

Table 1: Prevalence of human hydatidosis based on the hospital reports in different parts of Iran

City (Province)	No. of Patients	Years	Highest rate (yr)	F/M (%)	References
Hamadan (Hamadan)	55	1982-1992	20-39	61.8/38.2	(9)
Arak (Markazi)	250	1991-1997	10-49	60.8/39.1	(10)
Babol (Mazandaran)	24	1991-1996	41-60	50/50	(11)
Yazd (Yazd)	67	1991-1997	55-80	64.1/35.8	(12)
Urumia (West Azerbaijan)	202	1991-2001	16-50	65.8/34.1	(13)
Mashhad (Khorasan Razavi)	1759	1980-2002	20-29	57.2/42.9	(14)
Kashan (Esfahan)	85	1993-2000	20-29	55.3/44.7	(15)
Ahwaz (Khuzestan)	40	1994-2000	Children under 15	40/60	(16)
Tehran (Tehran)	31	1995-2005	children	42/58	(17)
Tabriz (East Azerbaijan)	23	2001-2006	children	48/52	(18)
Tehran (Tehran)	78	2001-2004	32-40	56.5/34.5	(19)
Zahedan (Sistan and Baluchistan)	49	1990-2005	-	25/75	(20)
Tehran (Tehran)	60	1984-2004	30-39	53.3/46.7	(21)
Khorram abad (Lorestan)	39	2002-2006	11-40	56.6/43.4	(22)
Hamadan (Hamadan)	179	1999-2006	20-39	55.9/44.1	(23)

Table 2: Reported cases of human hydatidosis in different organs of the body except liver and lung

Location	Age (yr)	Sex	City (Province)	References
Orbit	16	M	Ahwaz (Khuzestan)	(24)
Heart	32	M	-	(25)
Cerebellum	8	M	Tehran (Tehran)	(26)
Spleen	20	M	Bushehr (Bushehr)	(27)
Muscular	64 32 80	M M M	Ahwaz (Khuzestan)	(28)
Parotid gland	10	M	Nahavand (Hamadan)	(29)
Tibia	71	F	Ahwaz (Khuzestan)	(30)
Multifocal skeleton	53	M	Bushehr (Bushehr)	(31)
Urinary tract	11 cases (Dif-ferent ages)	-	Tehran (Tehran)	(32)
Pancreas	30	M	Tehran (Tehran)	(33)
Endocardial	45	M	Shiraz (Fars)	(34)
Multifocal and Mul-tiorgan	5	F	Tehran (Tehran)	(35)
Disseminated in-traspine	60	M	Tehran (Tehran)	(36)

Table 3: Seroprevalence of human hydatidosis in different regions of Iran

City (Province)	%	Method	References
Tehran (Tehran)	9.7	IFA	(37)
Nomadic tribes (Southern Iran)	5.4	ELISA & CIE	(38)
Lordegan (Chahar Mahal va Bakhtyari)	21.4	Casoni test	(39)
Tehran (Tehran)	5.9	IFA	(40)
Different cities (Chaharmahal va Bakhtyari)	4.8	CIE	(41)
Zanjan (Zanjan)	3.0	ELISA	(42)
Ilam (Ilam)	1.2	Dot-ELISA	(43)
Sanandaj and Divandareh (Kurdistan)	7.3	IFA	(44)
Kashan (Esfahan)	2.4	IHA	(15)
Different cities (Golestan)	2.34	IFA	(45)
Nomads (Khuzestan)	13.8	ELISA	(46)

Table 4: Prevalence of *E. granulosus* in autopsied stray dogs in different territories of Iran

Prevalence (%)	Provinces and regions	References
50.5	Esfahan	(63)
26.74	Tehran	(64)
22.3	Northern region	(65)
33.3	Fars	(66)
6.8	Kerman	(67)
49	Hamadan	(59)
5.0	Kerman	(60)
36.19	Fars	(68)
48	Tehran	(69)
19.1	Western Iran	(61)
12.3	Esfahan	(70)
44	Kurdistan	(44)
22	Khorasan Razavi	(62)

Table 5: Prevalence of hydatidosis in cattle, sheep, and goat based on abattoir data

Province	Cattle (%)	Sheep (%)	Goat (%)	Buffalos (%)	References
Fars	-	-	-	70	(71)
Kerman	7.2	9.2	6.8	-	(72)
Isfahan and Yazd	-	-	-	70	(73)
Hamadan	25.9	27.5	16.1		(74)
Yazd	-	-	-	39	(75)
Kerman	-	-	-	25	(75)
Sistan va Baluchistan	-	-	-	22	(75)
Hamadan	15.3	10.6	1.7	-	(76)
North Khorasan	26.9	20.6	7.4	-	(77)
Western Iran	16.4	11.1	6.3	12.4	(61)
Kerman	8.5	5.1	7.8	-	(78)
Kurdistan	28.02	51.9	-	-	(44)
Ardabil	38.3	74.4	20	11.9	(79)
Qom	3.5	9.3	2	-	(80)

Conclusion

Hydatidosis must be considered as a dilemma in Iran in terms of health policy because of its endemicity in the country (2, 53). However one point acknowledged by nearly all researchers in the country is that the rate of human and animal cases is decreased in comparison to a decade ago. A new study conducted here shows that the incidence of human hydatidosis in 2002 as 0.72/10,000 has decreased to 0.54% in 2006 (47). Improving of sanitation, health education, increasing the people knowledge of public health and improving the mechanism of slaughterhouses in many cities are considered as the most important reasons in this regard. Recently, the government has established a kind of Veterinary Police as watching forces in monitoring the sacrifice ceremonies. In parallel, an expert team affiliated to Iranian Veterinary Organization is ready in all places to present aid to peo-

ple in all aspects embracing the circle of scarified animal and society health. All services presented by these agents are free of charge to persuade people to cooperate with them.

It is worth mentioning that here is a tendency by most of the surgeons to treat human hydatidosis by chemotherapy instead of surgery or exploit a kind of “watch and wait” method and only some complicated cases being operated (Discussions in internal congresses). This leads to the decrease of number of patients via hospital data and accordingly a precise and detailed study should be conducted to throw light on this arena.

Of course, like other infectious diseases, hydatidosis must be regarded as an important issue in health policy makers' decisions. To date, an all through control programme has not been conducted, an issue,

when regarding Iran as an endemic area, sounds imperative and urgent.

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