

# Research in Veterinary Science and Medicine



Parasitology Review Article

# Review of Dirofilaria spp. infection in humans and animals in Iran

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#### ABSTRACT

Dirofilariasis is a metazoonoses transmitted by certain mosquito genera (Culicidae: Diptera). Chiefly canids are the reservoirs of Dirofilaria spp. This article analyzed all published records and researches relevant to Dirofilaria in Iran, to provide a basis for future studies in Iran and around the world. All of the important data from human and animal cases that included the pathogen and its reservoir, dispersion, and retrospective studies were investigated and analyzed. Furthermore, the natural history of parasites, pathogenicity, diagnosis, treatment, control, and the final status of the disease in the world was briefly mentioned. Two species of the genus Dirofilaria, Dirofilaria immitis (canine heartworm) and Dirofilaria repens, are detected in Iran. Till now, 13 human cases have been formally reported including seven subcutaneous and three ocular cases of D. repens, a four cases of D. immitis, including a rare case in testicular hydrocele, one ocular and one pre-ocular, a subconjunctival and two pulmonary cases suspected to be D. immitis. Animal and human infections have been recorded in 11 provinces of Iran. Different investigators have reported D. immitis in dogs (with the frequency of 0.95-62.8%), jackals (2.5 57.4%), foxes (5.7-50%), wolves (20-50%), and cats (0.8%) and D. repens in dogs (1.4-60.8%) and jackals (10%) in different areas of the country. The reports on Dirofilaria in Iran are to some extent scattered as regarded to distribution and other features of the disease. More studies should be taken in dirofilariasis in Iran, specifically in regions from where there are no reports.

Keywords: Dirofilaria, Dirofilaria immitis, Dirofilaria repens, Nematoda, Iran

# INTRODUCTION

Dirofilariasis or dirofilariosis is transmitted by mosquitoes (Culicidae: Diptera) and it is a metazoonotic disease.[1] Mostly canids are primary hosts to Dirofilaria spp. and they act as the reservoirs. This Dirofilariinae subfamily contains 10 genera, of which one is a pathogen for reptilians, one for aves, and the others are mammalian pathogens. Most species of Dirofilaria are transmitted by mosquitoes, while Dirofilaria ursi found in the brown bears is transmitted by the flies of family Simuliidae. [2,3]

The genus Dirofilaria has at least 27 species in two subgenera which infect 111 mammalian species. Of these, two species of Dirofilaria are more important in human and veterinary medicine. The Dirofilaria subgenus includes Dirofilaria immitis (canine heartworm) and Nochtiella subgenera Dirofilaria repens.[3,4]

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Dirofilariosis, which is caused by D. immitis, has been reported from almost every tropical, subtropical, and temperate region of the world. It is more prevalent in North America, South America, Australia, Japan, and Italy.[3,5] D. immitis is a nematode and its microfilaria is 258  $\pm$  7  $\mu$ m long, infectious L<sub>3</sub> larva is 0/75–1/3 µm long, and the mature worm is about 250-300mm. Its reservoirs are dogs and other members of Canidae such as wolf, fox, jackal, dingo (Australian wild dog), coyote (North American desert wolf), and occasionally other mammals such as the domestic cats, bear, seal, deer, panda, horse, rabbit, and primates such as the orangutan.[2,3]

D. repens has been reported from 36 countries around the world. Italy is one of the most important focuses of this disease. [3,4] The microfilaria of *D. repens* is 290  $\pm$  20  $\mu$ m long, infectious L3 larva is 0/64-1/08 mm long, [2,3] and the mature worm is about  $100-170 \times 0/4-0/7$  mm.<sup>[3,6]</sup> Mostly dogs are reservoirs of this species but in some cases, it was isolated from cat, lion, and fox. Humans are usually infected with Dirofilaria by accident and the parasite life cycle cannot be completed in human. A species that was named Dirofilaria conjunctiva previously is a synonym of *D. repens.* [3,6]

More than 77 mosquito species of Culex, Ochlerotatus, Anopheles, Aedes, Coquillettidia, Mansonia, Psorophora genera, and probably Culiseta are known to play the role as the intermediate host. [3,4,7,8] and are vectors especially for canine heartworm causing agent D. immitis. Around 20 mosquito species are vectors and intermediate hosts of D. repens. [3,9] In recent years, due to people traveling to non-endemic regions and moving disease reservoirs to nonendemic areas, case reports show an alarmingly growing trend. The reported cases around the world are usually much less than real human and animal infection cases.[3,10] Therefore, this disease is classified as an emerging zoonotic disease.[3,4]

It has been more than 36 years since the first dirofilariasis case was reported from Iran<sup>[3,11]</sup> and the World Health Organization in 1984 identified Iran as an infected region.[3] During years until 2020, lots of studies have been conducted and numerous animal and human cases have been reported.

In this review, we tried to survey any previous researches, reports, and information related to human and animal cases in Iran retrospectively. Variables including parasite species, animal host, dissemination, infection percentage, and human cases extracted and processed. Furthermore, the parasite life cycle, pathogenesis, diagnosis, treatment, and control are briefly reviewed.

# **MATERIAL AND METHODS**

In this study, the information obtained from the search databases of Scientific Information Database, Irandoc, Civilica, Magiran, Scopus, PubMed, and Google Scholar were used. Through advanced search, it was possible to search for articles with the keywords "Iran" and "Dirofilaria." Furthermore, the presence of the word Dirofilaria was included in the title of the mandatory search settings, and the search was performed by considering the year of publication as the next filter. For example, in the Scopus database, the latest information in this field is related to a case report from the south-eastern of Iran. [12] Furthermore, by reviewing the search databases of Irandoc, Civilica, and Google Scholar, it was possible to include thesis, books, and abstracts of articles published in national and international congresses in the field of this study. By researching in these databases, important information about dirofilariasis in Iran was obtained and analyzed by comparison of interprovincial, intercity, and interspecies types in the following and presenting the latest status of the disease in the world was briefly mentioned.

#### **RESULTS**

# Evolution of the parasite

Career mosquitoes receive microfilaria of Dirofilaria while blood feeding from peripheral blood containing the microfilaria of reservoirs. The worm grows and develops in the Malpighian tubules of the mosquito. This is the distinguishing feature of the genus Dirofilaria from others because the others often grow and develop in the flight muscle in chest or fat body cells of mosquito intermediate hosts. After about 2 or 3 weeks (according to environmental factors, especially temperature and mosquito genus), extrinsic incubation period has been passed and infective third-stage larva appears and migrates to the head and proboscis of the mosquito and while blood feeding, by perforating the lower lip proboscis, infects the next host through the created break or by actively perforating the skin. Forth stage larva, adult worms (male and female), and eggs are found in the body of the vertebrate host. The female worm is ovoviviparous. It takes about 7-9 months to observe an adult worm in the pulmonary artery and heart and microfilaria in peripheral blood in an infected dog. The worm life cycle is about 7 years and the reproduction period is 2-5 years in the body of a dog. D. repens genus life cycle is very similar to D. immitis.[1-3] Microfilaria of D. immitis shows subperiods and this was examined in dog's blood samples in Tehran<sup>[13,14]</sup> and Tabriz<sup>[15,16]</sup> and Golestan. [3,17]

# **Pathogenesis**

Microfilariae have not been observed in peripheral blood of humans and the adult stage is observed 6 months after infection with third-stage larva. Infertile adult and immature D. immitis genus stages have been observed in pulmonary artery and lungs, and in one case, fertile female has been observed in the lungs of a man with lymphoid leukemia. About 65% of pulmonary infection is asymptomatic. Furthermore, cough, chest pain, fever, and inquietude are the symptoms of this disease. D. repens is usually found as painful subcutaneous nodules around or inside the eyes, male genital system, and rarely in lungs. The mature form has also been found in the chest. The subcutaneous nodules are caused by host defensive reactions and they might be soft or hard. These nodules may be painful on palpation or pressure [Figure 1]. Eye infection causes redness, epiphora, blepharitis, pain, and itching. The best and safest way to diagnose infection in humans is to bring out the nodules and study on morphological properties of the worm. [3,4,6] The life cycle of *D. immitis* and *D. repens* shown in [Figures 1 and 2], respectively.[18,19]

# Diagnosis

Clinical signs of dirofilariosis are variable in dogs and include asymptomatic stage to mild symptoms such as cough, immobility, premature fatigue, and severe symptoms such as anemia, cardiac complications, and death. Blood tests by modified Knott's method, serological tests as ELISA and IFA, and molecular methods (PCR) can detect disease and infected dogs. [3,4] Farzaneh has reviewed clinical aspects of dirofilariasis in dogs in 1991[3,20] and Rafii has studied it on practical clinical aspects in 1996.[3,21] In 2012, Tabrizi stated that cases with dirofilariasis have a higher level of total bilirubin, alkaline phosphatase, and indirect bilirubin in comparison with non-infected cases that show that Dirofilaria can cause side effects on the liver, bile duct, and red blood cells.[22] Mahdizadeatar has referred to complications and symptoms of the disease, its diagnosis and treatment methods in 1991 and 1992.[3,23,24] Vahedi (1997) has reviewed various dirofilariasis diagnosis methods in humans and dogs. [3,25] Eslami et al. (2003) referred to the symptoms and treatment of the disease. [3,26] Ranjbar-Bahadori and Eslami (2005) compared two methods of diagnosing dirofilariosis, namely, modified Knott's and ELISA in dogs in Golestan Province. [3,17] A study by Sharifdini (2012) discovered that the infection rate of *D. immitis* in dogs more than 2 years old is higher than others in Meshkinshahr, Iran.<sup>[27]</sup> Jalali et al. (2016) recognized the outbreak of D. immitis by counterimmunoelectrophoresis besides modified Knott's method in 2013. [28] Zarei et al. accomplished the molecular method based on cytochrome oxidase subunit 1 gene to find out the prevalence of dirofilariasis. [29] Ranjbar-Bahadori et al. (2007) compared the specificity and sensitivity of two diagnostic methods of D. immitis (modified Knott's, Antigen Detecting Test Kit), and the McNemar (a statistical test used on paired nominal data) test showed that although the sensitivity of the second one was higher, differences were not significant (P > 0.05). Either in comparison of ELISA and immune complex disease (ICD) method, they stated that the ICD

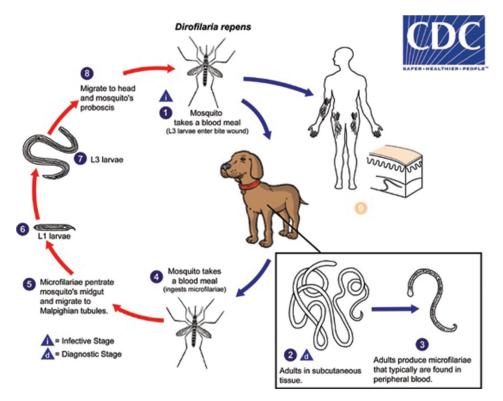


Figure 1: Dirofilaria repens life cycle. [19] https://www.cdc.gov/parasiteWWWs/dirofilariasis/biology\_d\_repens.html

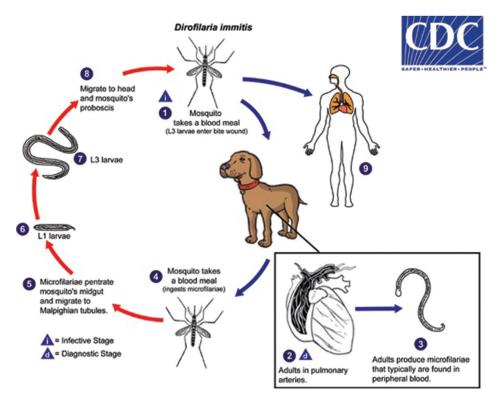


Figure 2: Dirofilaria immitis life cycle. [18] https://www.cdc.gov/parasites/dirofilariasis/biology\_d\_immitis.html

method is not recommended for the beginning of diagnosis, it may be a valuable secondary way for detecting dirofilariosis in dogs.[31]

# **Treatment**

The most practical human treatment is the surgical removal of a nodule with a nematode, and chemotherapy is not recommended, since the worm is often dead inside the nodule, and no microfilaria is found in the human peripheral blood. In dogs, thiacetarsamide or melarsomine and ivermectin, milbemycin oxime, or levamisole are used as a filaricide and a microfilaricide respectively.<sup>[3,4,64]</sup> In Iran, melarsomine in 2.5 mg/kg and ivermectin in 0.05 mg/kg have been used successfully in the treatment of dirofilariosis in cats.[3,48]

#### Control

Control and reduction of human dirofilariasis (HD) depend on the reduction of the infection of its reservoir hosts. Infected dogs should be treated with nematicides after accurate diagnosis. In endemic areas of the disease, treatment of all infected reservoirs (domestic and wild) should be on the agenda. Furthermore, chemoprophylaxis (using drugs for prevention) with the use of ivermectin should be used. It is important to inform and create awareness among dog owners about ways of transmission and preventing it. Reducing the population of mosquitoes and their larvae and personal protection of individuals and dogs against mosquito bites is effective in reducing human and animal infection. [3,4]

#### HD in Iran

Among the human cases of the disease, we can mention one case of eye infection of D. repens in Tehran,[3] one case in Mazandaran,[32] two cases of subcutaneous infection in Bandar Anzali and Lahijan,[33] and one case in Karaj (Tehran Province).[3,34] One rare case of testicular hydrocele infection with D. immitis in Bandar Abbas (Hormozgan Province)[35] and a subcutaneous dirofilariasis case of an Iranian man who traveled to Belgium have been reported. [36] Two pulmonary cases (probably D. immitis) based on the observation of coin lesion on radiography and also several cases of subcutaneous dirofilariasis from Ardebil Province have been reported.[37] There was an unreported eye infection of D. immitis from Gonbad (Mobedi, personal communication).[3] Maraghi et al. (2006) reported three cases of human infection with the D. repens in Ahvaz, two of which were diagnosed as subcutaneous nodules and the last, as an eye infection.[38] Tavakolizadeh and Mobedi (2009) presented the first report of ocular dirofilariasis in Tehran, by adult female D. repens worm in 2009.[39] Parsa et al. reported ocular infection with D. immitis by the molecular characterization method in Kerman in 2020.[12] Ashrafi et al., 2010, reported a subcutaneous nodule of D. immitis in Gilan that was suspected as cutaneous fascioliasis. [40] A paranasal subcutaneous nodule of D. repens was reported in Ahvaz from a 31-year-old man.[41] Tabatabaei et al. (2017), a case with the sub-conjunctival presence of D. immitis was detected in Tabriz. [42] Maraghi, 2019, discovered breast dirofilariosis with D. repens in a 40-year-old woman resident of Khuzestan.[43] Furthermore, Mirahmadi et al. (2017) reported ocular dirofilariasis by D. immitis in a 2-year-old child in Chabahar city located at Sistan and Baluchestan Province.[44] Negahban et al. (2007) presented a case with a subcutaneous nodule of D. immitis in Shiraz that was obtained with the fine needle aspiration method. [45] Tafti et al. (2010) discovered an ocular dirofilariasis by D. repens in Tehran. [46] Dirofilaria prevalence in human in Iran reported summarized in [Table 1].

#### Animal dirofilariosis in Iran

In Iran, animal dirofilariosis has been reported in dogs, jackals, foxes, wolves, and cats. D. immitis has been detected in all the animals above. However, D. repens was only found in dogs and jackals [Table 1].

The prevalence of *D. immitis* in a global study shows (11.45%) a total weighted prevalence in Iran. [47]

The first natural infection in stray dogs with D. immitis and D. repens in the country was reported in 1969 in Mazandaran Province, Tonekabon (former Shahsavar).[11] In that year, infection with D. immitis was seen in a domestic dog imported to Iran from the United States.<sup>[50]</sup> Darijani et al. (2009) presented the first report of Dirofilaria in domestic dogs in Kerman.<sup>[51]</sup> For the 1<sup>st</sup> time, the animal epidemic form of dirofilariosis infection in dogs was reported in the western villages of Meshginshahr, Iran city with 26.7% infection.<sup>[3,52]</sup> Alborzi et al. (2010) reported a domestic short hair cat, 2.5 years old in Ahvaz, Iran, with D. immitis confliction.<sup>[53]</sup> In a study, the prevalence of D. immitis evaluated with modified Knott's and immunochromatography was 10% and 11.7%, respectively.[54]

Various researchers from Fars, Khuzestan, Ardebil, Tehran, West Azerbaijan, East Azerbaijan, Golestan, Garmsar, Gilan, Kerman, Kermanshah, Chaharmahal-Bakhtiari, Sistan and Baluchestan, Hamedan, and Mazandaran Province have reported infections in dogs with D, immitis with the frequency of 0.95-62.8% and in Tehran, Khorasan Razavi, Mazandaran infection with *D. repens* was reported 1.4-60.8% [Table 2].

In 2004, Moulavi reviewed the micro-anatomy of parasites including D. immitis and D. repens in Iran. [3,55] In 2005, Lee and Wong introduced a new species Dirofilaria that the infected dog had lived in Germany and Iran before settling in the United States and being diagnosed, making it possible for it to become infected in Iran.[3,56]

Furthermore, in 1974, Javadian and Macdonald investigated the effect of D. repens species infection on Stegomyia aegypti (Aedes aegypti) mosquito egg production. Thus, one feeding from an infected dog statistically, significantly reduced egg production compared to mosquitoes fed from the blood of an uninfected dog.[3,57] So far, the species D. immitis has

Table 1: Prevalence of Dirofilaria in human and animals in Iran.					
Province	Dirofilaria immitis	Dirofilaria repens	Human infection	Animal infection	References
Ardebil	+	+	+	Dog, cat, fox, jackal	[3,29,49,52,58,59,65,66,67,68]
Chaharmahal-Bakhtiari	+	_	_	Dog	[69]
East Azerbaijan	+	-	+	Dog, fox, jackal, wolf, cat	[3,42,48,49,58,59,70-77]
Fars	+	+	+	Dog	[3,43,45,76-80]
Gilan	+	+	+	Dog, jackal	[33,40,59,81-84]
Golestan	+	_	+×	Dog, jackal	[17,58,59,81-83,85]
Hamedan	+	_	_	Dog	[86]
Hormozgan	+	_	+	Jackal	[3,35,59,87-89]
Kerman	+	_	+	Dog	[12,51,90-92]
Kermanshah	+	_	_	Dog	[93]
Khorasan Razavi	+	+	_	Dog	[3,94-96]
Khuzestan	+	+	+	Dog, cat, jackal, fox	[3,38,41,43,54,58,59,97-104]
Mazandaran	+	+	+	Dog, jackal	[3,11,32,58,59,81-84,105,106]
Qazvin	+	_	_	Dog	[84]
Semnan	+	_	_	Dog	[107,108]
Sistan and Baluchestan	+	_	+	Dog	[44,91,109,110]
Tehran	+	+	+	Dog	[3,36,39,50,82,111,112,114]
West Azerbaijan	+	_	-	Dog, jackal	[3,59,115,117]

Species	Province	Location	Infection rate (%)	References
Dirofilaria immitis	Ardebil Meshkinshahr		20.87	[29]
			62.80	[65]
			7.90	[3,52,118-120
			36.80	[3,52,118-120
			23.07	[68]
	Chaharmahal and Bakhtiari	Shahrekord	1.49	[69]
	East Azerbaijan	(Jolfa, Kaleybar)	21.20	[71]
	,	Marand	15.90	[71]
			18.02	[121]
		Sarab	13.50	[73]
		Tabriz	30	[74]
			11.60	[70,121]
			20.02	[71]
			8.40	[3,122]
			31.60	[3,123]
			15	[75]
			14	[76]
		East Azerbaijan	14.70	[3,49]
		East Hzerouijan	30	[3,67]
	Fars	Shiraz	0.95	[3,80]
	Turo	Office	9.60	[3,78]
	Gilan	Gilan	51.42	[81,82]
	Ghan	Ghan	4.41	[83]
	Golestan	Golestan	15.38	[81,82]
	Golestan	Golestan	14.55	[3,17]
			18.18	[3,17]
			3.94	[83]
			15.45	[85]
	Hamedan	Hamedan	19.27	[86]
	Kerman	Kerman	2	[51]
	Kerman	Kerman	5.40	[90]
			5.40	
		Bam	5 15.15	[92]
	Kermanshah	Kermanshah	18.30	[91]
				[93]
	Khuzestan	Ahvaz	12.61	[100]
			5 8	[97]
				[99]
			8.70	[3,102]
	M 1	c :	10, 11.7	[54]
	Mazandaran	Sari	6	[105]
		Tonekabon	7.69	[81,82]
			4	[3,11]
		m 1.1	5.37	[83]
	0	Tonekabon	15	[106]
	Semnan	Garmsar	12.29	[107]
	0 15.1.1	7.1.1	5.20	[108]
	Sistan and Baluchestan	Zabol	27.50	[91]
	Tehran	Tehran	3	[82]
			2.30	[111]
			1.40	[3,124]
	West	(Targavar,	25	[116]
	Azerbaijan	Margavar, Kolshin,		
		and Hovarchin)		
		Uromie	3	[115]
			4	[3,115]

(Contd...)

Table 2: (Continued)				
Species	Province	Location	Infection rate (%)	References
Dirofilaria repens	Ardebil Khorasan Razavi Mazandaran	Meshkinshahr Mashhad Tonekabon	3.84 6.40 6.50 60.80	[68] [3,96] [3,95] [3,11]
	Tehran	Tehran	26 1.40	[3,11] [111] [3,113]

<b>Table 3:</b> Infection rate of <i>D</i>	irofilaria among jackals in Iran		
Species	Province (location)	Infection rate (%)	References
Dirofilaria immitis	East Azerbaijan	20, 57.1	[3,49,58,67]
,		57.4, 28	[77]
	Khuzestan	11.1	[3,58]
		28.5	[3,102]
	Golestan	12.5	[3,58]
	Mazandaran	10	[3,58]
	North Khorasan	8.9	[125]
	Zone 1*	3.8	[59]
	Zone 2**	2.5	[59]
	Zone 3***	5%	[59]
	11 Provinces****	7.5	[3,58]
Dirofilaria repens	Mazandaran (Tonekabon)	10	[3,11]

\*Gilan, Mazandaran, and Golestan, \*\*West Azerbaijan, East Azerbaijan, Ardebil, Markazi, and Esfahan, \*\*\*Khuzestan and Hormozgan, \*\*\*\*infected cases were in East Azerbaijan, Khuzestan, Golestan, and Mazandaran

been isolated in cats only once from Tabriz. From 234 cats, microfilaria was obtained in two cases (0/8%) of peripheral blood.[48] There are two official reports about identifying D. immitis in wolves in East Azerbaijan. The first was a reported infection of one out of five wolves (20%)[49] and the other was infection of one out of two.[3]

The first report of jackal infection to D. repens (10%) was in Mazandaran Province.[3,11] Jackal infection to D. immitis was reported from 2.5% to 57.4% in East Azerbaijan, Ardabil, Khuzestan, Golestan, and Mazandaran Provinces by different researchers [Table 3], but in 2003, the infection rate reported by Meshgi et al. in 11 provinces was 7.5% in total, that in East Azerbaijan, Khuzestan, Golestan, and Mazandaran Provinces, five out of 66 trapped jackals were infected. [3,58] Meshgi evaluated the prevalence of D. immitis in jackals and foxes in three areas of Iran. The infection rate in the first zone consisting of Gilan, Mazandaran, and Golestan was 3.8%. That of the second one (Zone 2, West Azerbaijan, East Azerbaijan, Ardebil, Markazi, and Esfahan) was 2.5% and the last one (Zone 3, Khuzestan and Hormozgan) was 5%.<sup>[59]</sup>

Infection of foxes with *D. immitis* has been recorded from East Azerbaijan, Ardabil, and Khuzestan Provinces by different researchers with an abundance of 5.7%-50% [Table 4], but in 2003, Meshgi et al. reported the rate of infection in six provinces as 9% in total so that two out of a total of 22 foxes caught in East Azerbaijan and Khuzestan Provinces were infected. They also mentioned an 8.9% infection of the total number of caught wild carnivores, including foxes, jackals, and wolves to D. immitis. Furthermore, Meshgi reported a rate of 8.1% in West Azerbaijan, East Azerbaijan, Ardebil, Markazi, and Esfahan for foxes infected to D. immitis. In the country, the species *D. repens* has not been isolated from foxes so far. [3,58]

# Dirofilaria infection in Iran

Dissemination of dirofilariasis in Iran: In total, human and animal Dirofilaria infection is reported from eighteen provinces of Iran. D. immitis species has been observed in all of the provinces of the country. In West Azerbaijan, Semnan, Khorasan Razavi, Kermanshah, Hamedan, Qazvin, and Chaharmahal-Bakhtiari Provinces, only animal infection has been reported. In Ardabil, Golestan, Gilan, Kerman, Khuzestan, East Azerbaijan, Fars, Hormozgan, Sistan and Balochistan, Mazandaran, and Tehran, both human and animal infections of this species have been reported. D. repens species was reported in five provinces. While in Khorasan Razavi Province, only animal infection was documented, in Tehran, Mazandaran, Khuzestan, Fars, Ardebil, and Gilan Provinces, both human and animal infections have been found [Table 1].

**Table 4:** Infection rate of *Dirofilaria* among foxes in Iran.

Province	Infection rate%	Reference
East Azerbaijan	5.7–11.1 13.3	[3,49,58,67] [77]
Khuzestan	50	[3,58,102]
6 Provinces*	9	[3,58]
Zone 2**	8.1	[59]

\*Infected cases were in East Azerbaijan and Khuzestan. \*\*West Azerbaijan, East Azerbaijan, Ardebil, Markazi, and Esfahan

According to [Table 1], in the seven provinces of Tehran, Gilan, Khuzestan, Fars, Ardebil, Khorasan Razavi, and Mazandaran, human or animal infection to both species of D. immitis and D. repens has been reported. Although in two other independent studies, neither of these two species were found in carnivores of Mazandaran Province. [3,60,61] Given that Ardabil (Meshginshahr)[3,37,52,55,62] and East Azerbaijan (Tabriz)[3,15,16,63] were introduced as two zoonotic centers of dirofilariasis (D. immitis), human cases were presented from both and but no cases of *D. repens* species were found in East Azerbaijan. None of the provinces reported human infection alone with *D. immitis*. It is worth mentioning that none of the two species of *Dirofilaria* were previously found in carnivores of Gilan Province.[3,60]

#### DISCUSSION

Due to the increase in human cases and also the higher prevalence of this disease in the northern regions of the country, human coexistence with animals is an important factor. In this regard, periodic attention to parasite testing and the use of antiparasitic drugs prescribed to animals should be taken seriously. The results indicate an increase in the incidence of *D. repens*, as well as an increase in conflict areas in more recent studies, which is more pronounced, especially in areas where health is not pursued more seriously. Furthermore, the number of cases of wild carnivores indicates the spread of this disease in this species of animals throughout the country, which is an important factor in the transmission in companion and domestic animals. Thus, attention to ecological measures in this regard is very important. It seems that in some parts of Iran which have been cleared of malaria or it has been controlled, dirofilariasis is one of the most important diseases transmitted by mosquitoes. However, there is no codified surveillance program for this disease, in the health and veterinary networks of the country. Due to the increasing trend of human reported cases of dirofilariasis in recent years, more attention from physicians and laboratory scientists to clinical symptoms of this disease is needed, especially in the centers of the disease or areas with significant animal infection. Most of the reports related to dirofilariasis in Iran were in terms of parasitology and isolation of parasites from animal reservoirs. Therefore, it is

necessary to study this disease in other parts of the country that has not been researched. The presence of stray dogs and other carnivores as reservoirs, the increasing phenomenon of keeping dogs and cats as pets in cities in recent years, the use of dogs in police forces to detect crimes and in Red Crescent organizations for the occurrence of emergencies, and the role of herding dogs in the agricultural economy of rural areas, demand more attention from health and veterinary authorities in the country to dogs and their common diseases with humans, especially dirofilariasis. There is no entomological information available about the carriers of this disease in Iran.

#### **CONCLUSION**

Statistical reports indicate the incidence of this infection in animal and human in 11 provinces of Iran. Conflict with D. immitis were in dogs ranged from 0.95 to 62.8%, jackals (2.5-57.4%), foxes (5.7-50%), wolves (20-50%), and cats (0.8%) in different researches. These reports have been reported for D. repens in dogs and jackals (1.4-60.8%) and (10%) in different regions, respectively. Reports of dirofilaria in Iran are scattered and with different pathogenic characteristics, which highlights the importance of further studies on dirofilariasis in Iran, especially in areas where there is no research history.

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# Declaration of patient consent

Patient's consent not required as patients identity is not disclosed or compromised.

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#### **Conflicts of interest**

There are no conflicts of interest.

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