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Review Article

A Systematic Review and Overview of the Prevalence of *Dirofilaria immitis* in Iranian Dogs in a 10-Year Period (2013-2023)

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Abstract

Introduction: Today, insect-borne diseases are increasing in the world due to climate changes, population growth, and the spread of marginalization in cities. Dirofilariasis is also considered one of the most important insect-borne parasitic diseases in the world, which can also be transmitted to humans and is considered one of the zoonotic diseases. *Dirofilaria immitis* is the most important type of dirofilariasis, which is a parasite of the circulatory system of humans and carnivores, especially dogs, which is known as dog heartworm.

Methods: This is a cross-sectional retrospective study. *D. immitis* is present in many parts of Iran, and the main purpose of this study is to investigate the research related to the seroprevalence of dirofilariasis in dogs in 10 years between 2013 and 2023 in Iran.

Results: According to the studies, the prevalence of dirofilariasis in dogs in this period in the studied provinces of Iran was found to be 16.59%. The highest prevalence of dirofilariasis in dogs is related to Gilan and Mazandaran provinces with 78.57% and 50% prevalence, respectively, and the lowest statistics were related to Isfahan province with 0.95% infection.

Conclusion: The results of this study revealed that there is a significant relationship between weather conditions and infection statistics. Furthermore, provinces with hot and humid climates have higher statistics, and provinces with desert and dry climates have lower statistics. This will be extremely effective in control programs.

Keywords: Systematic review, *Dirofilaria immitis,* Dogs, 10-year period, Iran

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Introduction

Every year, millions of new cases of parasitic diseases transmitted by insects are recorded in the medical and veterinary fields in the world, which can cause thousands of deaths annually (1). Dirofilariasis is also one of the most important diseases transmitted by insects, which is of great importance in veterinary medicine and medicine, and today, due to climate changes in the world, the geographic range of this parasite is expanding. *Dirofilariasis*, which is a zoonotic disease and is caused by filarial nematodes, has at least 27 different species that can infect and sicken 111 different species of mammals, the two main species of *Dirofilaria* are *Dirofilaria immitis* and *Dirofilaria repens*, which can cause the occurrence of mild or severe diseases. Dogs are one of the main hosts of dirofilariasis disease in the world, but humans can also be infected with this disease by accident, and there have been numerous reports of human cases of dirofilariasis in different countries. Dogs and some canids such as wolves, foxes, and jackals, cats such as domestic cats, rabbits, horses, and deer can also be reservoirs of *D. immitis* (2). *D. immitis*, which is an important species of *Dirofilaria*, and its world fame is dog heartworm, has the most cases of annual infections in tropical and subtropical regions due to the suitable climate for *Culicidae* mosquitoes which are among the most important foci of *D. immitis* disease in the countries of the American continent, Australia, Japan, and Italy (2,3). The main clinical symptoms of *D. immitis* in dogs are persistent cough, shortness of breath, lethargy, weight loss, and anemia, and in acute cases, it can cause heart failure and internal hemolysis of the pulmonary vessels, which can lead to death if not treated (4).

Materials and Methods

The search strategy and systematic review of published studies on the prevalence of Dirofilaria immitis in dogs between 2013 and 2023 in Iran is based on the (PRISMA) checklist. This is a retrospective systematic review and the

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main goal of this study is to collect and analyze statistical data related to dog heart disease during the years 2003 to 2023 in Iran.

Disease Status

Iran and the World

Today, dirofilariasis is an emerging tropical disease that can spread even with climate change. *D. immitis* was discovered for the first time in São Paulo in the southeast of Brazil in 1921, and it has been available in almost all parts of the world in the last three decades (5). Furthermore, the American continent is considered the first place to report dirofilariasis, which is regarded as one of the important centers of this disease today, and many types of dirofilariasis that do not exist in other parts of the world exist in the American continent, which requires more extensive research by researchers in this area. It is continental, and *Dirofilaria tenuis* which is one of the species of dirofilariasis is only specific to the American continent (6). Iran is also one of the countries where several cases of *D. immitis* are recorded almost every year; therefore, the investigation of this disease is of particular importance. It is even possible that this disease will spread over time in geographical areas where there is no report of *D. immitis* (7). *D. immitis* was reported and recorded in Iran for the first time in 1969, and the World Health Organization (WHO) registered Iran as one of the endemic areas for dirofilariasis in 1984 (2,8). There are different ways to diagnose the *D. immitis* parasite, but the main test methods for the seroprevalence of this disease in the world and Iran are polymerase chain reaction (PCR), Knott's test, and the enzyme-linked immunosorbent assay (ELISA). The studies conducted during 2013-2023 in Iran also show that the main method of laboratory diagnosis of *D. immitis* is the PCR laboratory method.

Life Cycle

Understanding and investigating the life cycle of *D. immitis* is of great importance. Canines are considered the main reservoirs of this parasitic disease, which are the most important factors in the life cycle of this disease. The life cycle of *D. immitis* has five larval stages that last between 99 and 152 days. Adult worms usually live in the pulmonary arteries, but they may also enter the right ventricle or right atrium, which is extremely dangerous for the animal. The length of adult female worms is between 230 and 310 mm, and their width is 350 micrometers. Furthermore, the length of adult male worms is 120 to 190 mm, and their width is 300 micrometers; in addition, male worms have uncoordinated spicules. Female worms release microfilaments (L1) into the blood after mating, and female mosquitoes of the *Culicidae* family enter the digestive system of the mosquito after biting and feeding on the microfilarial reservoir animal (L1) and migrate to the Malpighian tubes through hemocoel and midgut.

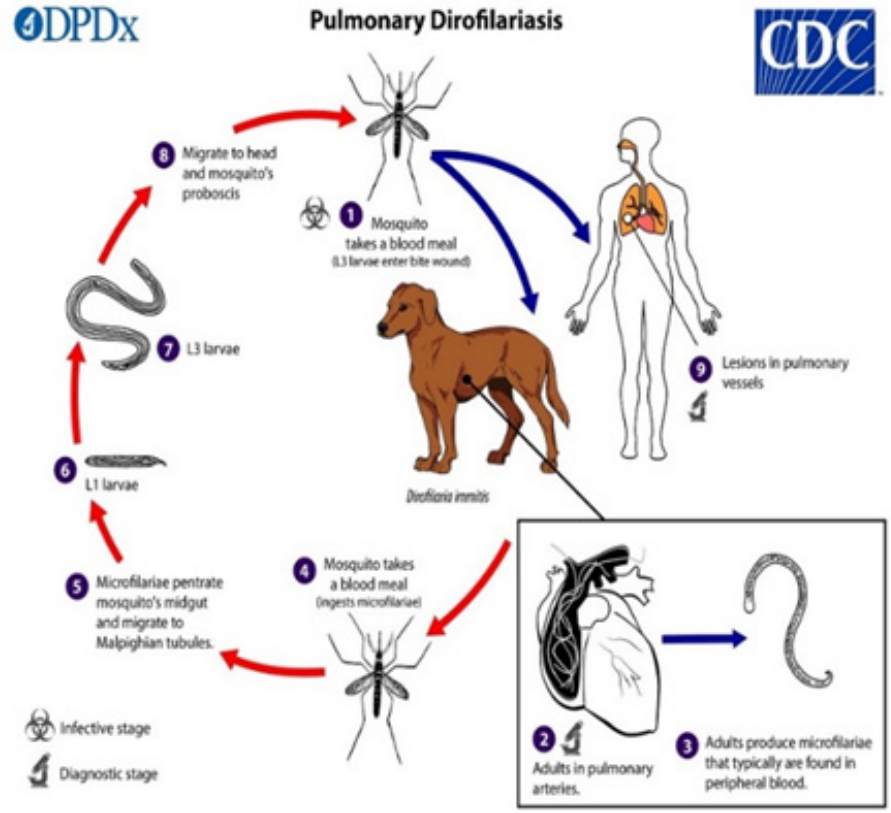

Figure 1. Life Cycle of *Dirofilaria immitis*. (*License* the Creative Commons Attribution-ShareAlike 4.0 International License ("CC BY-SA") and/or the GNU Free Documentation License ("GFDL"). Source: https://academic-accelerator.com/encyclopedia/dirofilaria-repens

Due to the suitability of weather conditions, after a period of 8 to 17 days, L1 will be transformed into L2 and L3 (pathogenic form) by molting twice, and they will migrate to the proboscis of the mosquito. The pathogenic form (L3) of the *D. immitis* parasite after the mosquito bite and entering the host's body in the fatty tissue under the skin turns into the L4 form, and then by turning into the L5 form, it migrates and moves toward the vascular system of the host's body (Figure 1). Then, the immature adult form becomes the mature form, and the adult form of *D. immitis* can live between 5 and 10 years (9).

Disease Transmission

In general, 70% of all organisms on the planet are insects. Mosquitoes are also considered insects, and humans and animals are in contact with these organisms throughout the day and night (1). Insects and especially mosquitoes are more resistant to environmental conditions due to their ability to fly, and considering that many infectious diseases in the world are transmitted by insects, especially mosquitoes, controlling these creatures is always one of the problems of organizations. It is hygienic. Most of the research conducted on *D. immitis* has been done on the reservoir agent, which is a mammal, but it should be noted that the agents of *D. immitis* spread and transmission are mosquitoes of the *Culicidae* family, and there is a strong connection between this disease and the distribution of mosquitoes. It is extremely difficult to obtain high-quality monitoring data on mosquitoes, but the environmental factors that affect the life of mosquitoes are of high value (10). This disease is transmitted by mosquitoes of the Culicidae family. Culicidae family mosquitoes have different genera. But in general, *Aedes spp., Armigeres spp., Culex spp., Anopheles spp*. are involved in the transmission of Dirofilaria immitis parasite (11,12).

Results

The results obtained from the statistical analysis of the studies conducted between 2013 and 2023 show that among the studies conducted in 10 provinces of Iran, the prevalence of dirofilariasis in dogs varies between 0.95% and 78.57%. In this 10-year period, among the 1850 examined dog blood serum samples, 307 samples were positive, which means that the average contamination of *D. immitis* in Iran is 17.40, and in the northern provinces of Iran such as Mazandaran and Gilan which are located on the edge of the Caspian Sea, the highest incidence of *D. immitis* in Iran has been recorded with 78.57% and 50%, respectively. One of the most important reasons for the high statistics in these areas is the suitable climatic conditions for the growth and reproduction of mosquitoes of the *Culicidae* family (13). From the total of 16 research studies, the PCR method was used 9 times, Knott's test method 6 times, and the ELISA method once (Table 1).

However, the statistics are extremely low in provinces with hot and dry climates and central Iran such as Isfahan and Kerman. The prevalence of contamination in Sistan and Baluchistan province (29.03%), Kerman province (6.72%), East Azerbaijan province (12.82%), Tehran province (28.29%), Hamedan province (4.45%), Isfahan province (0.95%), Lorestan province (6.93%), Mazandaran province (50%), Qazvin province (27.27%), Gilan province (78.57%) are depicted in Table 2 and Figure 2.

Table 1. Different Methods to Diagnose the *Dirofilaria immitis* Parasite (PCR, Knott's test, and ELISA)

Author Name	Year	Method	No of Samples	No of Positive Samples	Positive Percentage
Khedri et al (13)	2014	Knott's test	87	24	27.58
Khedri et al (13)	2014	Knott's test	33	5	15.15
Hosseinzadeh Varjoy et al (14)	2016	PCR	121	14	11.57
Raoof and Garedaghi (15)	2017	Knott's test	100	14	14
Bamorovat et al (16)	2017	ELISA	149	8	5.36
Bamorovat et al (16)	2017	PCR	149	6	4.02
Pedram et al (17)	2019	PCR	311	88	28.29
Anvari et al (18)	2019	Knott's test	99	30	30.30
Hashemzadeh Farhang et al (19)	2019	Knott's test	200	26	13
Hoseini et al (20)	2020	PCR	157	7	4.45
Naderi et al (21)	2021	Knott's test	100	10	1
Hosseini et al (22)	2022	PCR	105	1	0.95
Hosseini et al (22)	2022	PCR	101	7	6.93
Hosseini et al (22)	2022	PCR	66	33	50
Hosseini et al (22)	2022	PCR	44	12	27.27
Hosseini et al (22)	2022	PCR	28	22	78.57
Total	-	-	1850	307	16.59

*Note*PCR: Polymerase chain reaction; ELISA: Enzyme-linked immunosorbent assay.

Discussion

Statistical information and research conducted around the world demonstrate that dirofilariasis infection is spreading, and the reasons for this issue can be climate change, global warming, as well as the increase in insect populations in endemic areas. In this 10-year period, various studies and diagnostic methods have been conducted in Iran, most of which were related to the provinces of East Azarbaijan, Kerman, and Sistan and Baluchistan. So far, *D. immitis* has been reported in dogs, jackals, foxes, wolves, and cats in Iran (23). Almost all countries of the world are facing *D. immitis*, but the countries in the American continent, and especially the countries in Latin America record the most positive cases of this disease. The average incidence of *D. immitis* in Brazil and Argentina is 45% and 74%, respectively (24,25), but the average incidence of this disease in dogs in the United States varies between 1% and 12% (26). However, the incidence rate in the European continent is lower than that in the American continent, and the southern countries of the European continent have the highest incidence rate of *D. immitis* due to hot and humid weather conditions. The incidence rate in Spain is 19.4% (27), Portugal 2.1% (28), and Italy 6.1% (29). The incidence rate in the African continent which is one of the places with a dry climate varies between 1.4% and 14.5% (30). In 2023, Ying et al conducted a detailed statistical meta-analysis on *D. immitis* in China, showing that the infection rate is high in hot and humid areas, and it was also found that the infection rate is higher in old dogs, which can be attributed to the less movement of old dogs, and the lack of movement makes it easier and more frequent for mosquitoes of the *Culicidae* family to bite (3). In the past, mosquito-borne diseases have had a high value in Iran, and the most important ones have

Table 2. Prevalence of Dirofilariasis in Dogs in Different Provinces of Iran (2013-2023)

Province Name	No. of Samples	No. of Positive Samples	Positive Percentage
Sistan and Baluchistan	186	54	29.03
Kerman	431	29	6.72
East Azerbaijan	421	54	12.82
Tehran	311	88	28.29
Hamedan	157	7	4.45
Esfahan	105	1	0.95
Lorestan	101	7	6.93
Mazandaran	66	33	50
Qazvin	44	12	27.27
Gilan	28	22	78.57
Total	1850	307	16.59

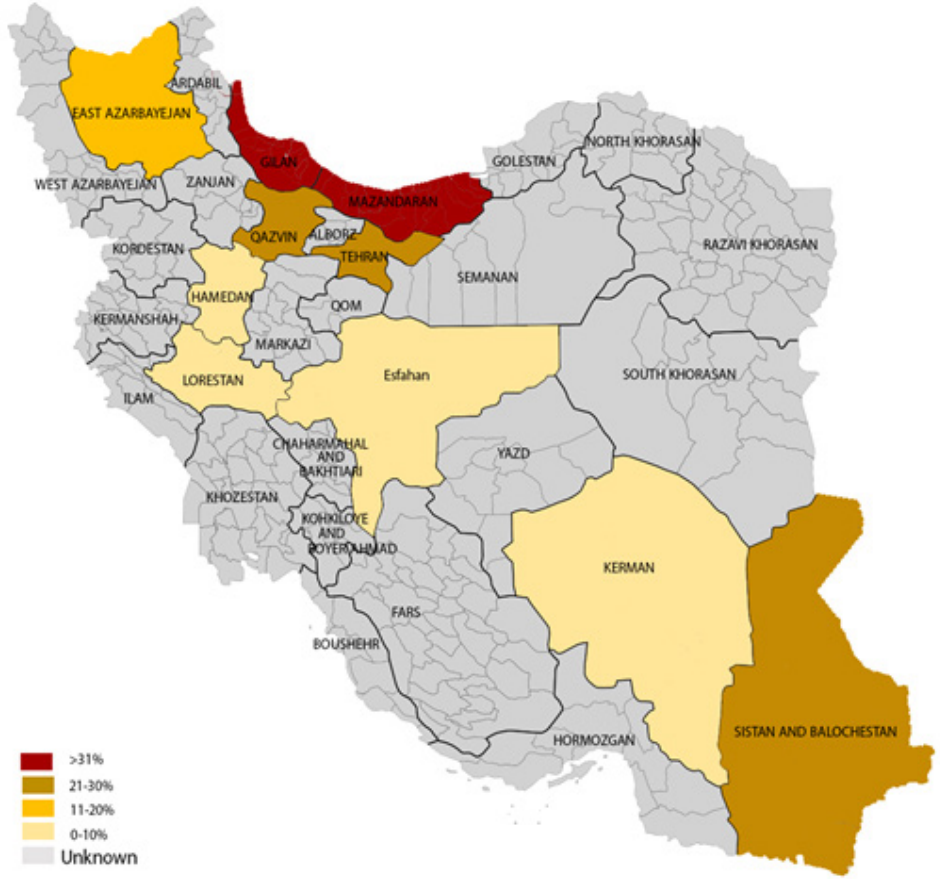

Figure 2. Distribution Map of *Dirofilaria immitis* between 2013 and 2023 in Iran

been malaria and leishmaniasis, which have been well controlled by careful health planning, and the number of infected people is close to zero, but leishmaniasis is still one of the problematic diseases in Iran (1). Nevertheless, currently, since both human and animal forms have been reported in Tehran, Khuzestan, Mazandaran, Ardabil, Gilan, and Fars provinces, dirofilariasis can be mentioned as one of the emerging zoonotic diseases in Iran, in which unfortunately there is still no detailed health and control plan by the Ministry of Health and Veterinary Organization for this disease. The best way to control this disease is to quickly treat infected dogs and clean the environment from infected mosquitoes according to environmental laws (31,32). Accordingly, we hope to move toward the definition of a detailed control program day by day with review research and systematic reviews.

Authors' Contribution

Conceptualization: Yagoob Garedaghi, Alireza Ghorbani.
Data curation: Yagoob Garedaghi.
Formal analysis: Yagoob Garedaghi.
Investigation: Alireza Ghorbani, Raha Jannati.
Methodology: Alireza Ghorbani.
Project administration: Alireza Ghorbani.
Resources: Alireza Ghorbani, Raha Jannati.
Supervision: Yagoob Garedaghi.
Validation: Yagoob Garedaghi.
Visualization: Alireza Ghorbani.
Writin–goriginal draft: Alireza Ghorbani.
Writing–review & editing: Yagoob Garedaghi.

Competing Interests

All authors have no conflict of interest to report.

Ethical Approval

Not applicable.

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