THESIS

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The Prevalence of Feline Heartworm Disease in Hungary

A Macskák Szívférgességének Előfordulása Magyarországon

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Abstract

Feline heartworm disease (FHW), caused by the parasitic nematode *Dirofilaria immitis*, is an emerging health concern for cats, especially in regions where environmental conditions favor the proliferation of mosquito vectors. While research has extensively focused on canine heartworm disease, FHW remains both underdiagnosed and underreported in cats due to its often subtle and nonspecific clinical presentation, despite its potentially severe outcomes.

This thesis investigates the prevalence of FHW in Hungary, a country with limited data on the disease, where rising temperatures and shifting vector populations suggest an increasing risk of infection. The study employs a comprehensive literature review alongside serological testing, particularly antibody tests, of cats from various regions to assess the prevalence of feline heartworm infection.

The negative antibody test results obtained from the sampled feline population raise important questions about the actual prevalence of heartworm disease in Hungary, as these results could suggest low exposure rates or reflect the limitations of antibody testing. While antibody tests are essential for identifying heartworm larvae exposure and prior exposure to the parasite, they may fail to detect current infections, particularly in populations with only adult worms or those in early stages.

This research emphasizes the need for a multifaceted diagnostic approach to obtain a more accurate understanding of the disease's prevalence and to identify at-risk populations. The thesis highlights the importance of raising awareness among veterinary practitioners and pet owners regarding the implications of serological testing results, as well as the need for comprehensive prevention strategies. Ultimately, this study aims to enhance knowledge of feline heartworm disease in Hungary and advocate for improved diagnostic protocols to protect feline health.

Absztrakt

A macskák szívférgessége (FHW), amelyet a *Dirofilaria immitis* parazita fonálféreg okoz, egyre növekvő egészségügyi problémát jelent a macskák számára, különösen azokban a régiókban, ahol a környezeti feltételek kedveznek a szúnyogvektorok elszaporodásának. Míg a kutyák szívférgessége körüli kutatások széleskörűen zajlanak, a FHW a macskák körében aluldiagnosztizált, mivel klinikai megjelenése gyakran diszkrét és nem specifikus, annak ellenére, hogy potenciálisan súlyos következményekkel járhat.

Ez a dolgozat a FHW előfordulását vizsgálja Magyarországon, ahol a betegségről korlátozott adatok állnak rendelkezésre, és ahol a növekvő hőmérsékletek és a vektorpopulációk változása egyre nagyobb kockázatra utal. A dolgozat átfogó irodalmi áttekintést tartalmaz, valamint az általunk elvégzett szerológiai tesztek (különösen antitest-tesztek) eredményeit, a különböző régiókból származó macskákon.

A megvizsgált macskák populációjából nyert negatív antitest-teszt eredmények fontos kérdéseket vetnek fel a szívférgesség valódi előfordulásával kapcsolatban Magyarországon, mivel ezek az eredmények alacsony kitettségi arányokat sugallhatnak, vagy a szérum antitest-tesztek korlátait tükrözhetik. Bár az antitest-tesztek elengedhetetlenek a szívférgek lárváinak való kitettség és a parazita korábbi kitettségének azonosításához, előfordulhat, hogy nem képesek észlelni a jelenlegi fertőzéseket, különösen olyan populációkban, ahol csak felnőtt férgek találhatók, vagy ahol a korai stádiumú fertőzések vannak.

Ez a kutatás hangsúlyozza a több szempontú diagnosztikai megközelítés szükségességét a betegség előfordulásának pontosabb megértése érdekében, valamint a kockázatos populációk azonosítása érdekében. A dolgozat kiemeli, hogy fontos felhívni a figyelmet az állatorvosi szakemberek és a háziállattartók körében a szérum tesztelési eredmények következményeire, valamint a átfogó megelőzési stratégiák szükségességére. Végső soron a tanulmány célja, hogy növelje a macskák szívférgességével kapcsolatos ismereteket Magyarországon, és előmozdítsa a diagnosztikai protokollok javítását a macskák egészségének védelme érdekében.

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ABBREVIATIONS

FHW – Feline Heartworm disease

D. immitis – *Dirofilaria immitis*

HARD – Heartworm-Associated Respiratory Disease

L1/2/3/4/5 – first/second/third/fourth/fifth larval stage

DV view – dorsoventral view

VD view – ventrodorsal view

INTRODUCTION

Heartworm disease, caused by parasitic worms of the genus *Dirofilaria*, has traditionally been a major health concern for dogs in warm and humid climates [1]. However, in recent decades, the geographic range of this parasite has been expanding, posing a growing threat to canine populations in previously unaffected regions.

This extends to Hungary, that was historically considered free from endemic canine heartworm disease caused by *Dirofilaria immitis*, with its continental climate. However, rising temperatures associated with climate change have facilitated the establishment of this parasite, leading to a significant increase in diagnosed canine cases since the late 2000s [2]. This trend highlights the dynamic nature of parasite-host interactions and the potential for geographic range expansion.

Cats, though considered imperfect hosts for *D. immitis*, are susceptible to infection. Unlike dogs, who typically harbor a higher parasite burden and develop more pronounced clinical signs, feline infections are often characterized by limited worm development and few or transient clinical signs that can be easily overlooked [3]. This, coupled with the historically low prevalence of canine heartworm disease in Hungary, has likely resulted in underdiagnosis of feline infections. Feline heartworm infections occur wherever canine heartworm is found, with cat prevalence at about 10% of dog prevalence [4].

This thesis aims to shed light on the current status of this potential threat to feline health regarding feline heartworm disease in Hungary by investigating its prevalence, risk factors, and distribution through a comprehensive analysis of existing literature, clinical data, and epidemiological surveys. By examining the status of feline heartworm infection in Hungary, this research seeks to provide valuable insights into the dynamics of disease transmission, identify vulnerable populations and ultimately, this study contributes to the broader understanding of the global epidemiology of feline heartworm disease and informs targeted strategies for prevention and control in Hungary and similar regions.

LITERATURE REVIEW

2.1 PATHOGENESIS

2.1.1 Transmission

The pathogenesis of feline heartworm disease begins when infectious larvae are transmitted via mosquito bites. These larvae then migrate through the host's body, maturing into adult worms that eventually lodge in the pulmonary arteries and sometimes the heart. Although cats are not the natural hosts for *Dirofilaria immitis*, they can still become infected, highlighting the importance of understanding the life cycle and transmission dynamics of these parasites.

Studies suggest that heartworm infections can impact cats regardless of age or overall health, including those with intact immune systems or suppressed ones. Both indoor and outdoor cats are at risk of being infected [5]. Earlier research suggested a higher prevalence of heartworm infection in male cats compared to females. However, more recent studies have challenged this notion, showing no significant differences in infection rates based on gender, indicating that both male and female cats are equally susceptible to heartworm infection [6].

Transmission occurs exclusively through infected mosquitoes, which act as biological vectors. During a blood meal, a female mosquito ingests microfilariae present in the bloodstream of an infected host. These microfilariae are unable to develop into adult worms without further maturation within the mosquito. After ingestion, they migrate to the mouthparts of the vector, where they develop into their L3 larvae. This typically takes 10 to 14 days at temperatures above 27°C [1], [4]. However, when temperatures fall below 14°C, larval development ceases, establishing an important limitation on the transmission of the disease [7]. Once a cat is bitten by an infected mosquito, the L3 larvae are released into the wound, initiating the infection.

2.1.2 Life cycle

After transmission to the host, once the L3 larvae enters the cat’s bloodstream, they migrate into the subcutaneous tissues, where they begin their development. It typically takes a 3 days post-infection for the L3 to develop into the fourth larval stage [8]. During the next 2 months, the L4 larvae will continue to migrate through the subcutaneous and muscular tissues, undergoing essential metabolic changes to prepare for entry into the vascular system [3].

As the larvae develop into the fifth larval stage, the immature adult stage, they enter the vascular system, primarily targeting the peripheral veins. They then migrate toward the right side of the heart and eventually settle in the pulmonary arteries, which generally takes between 70 to 90 days after the initial infection [3]. Unlike dogs, where multiple larvae can mature into dozens of adults, cats typically harbor only 1 to 6 adult worms. This is due to their stronger immune response, which results in a higher mortality rate among the larvae, preventing many from reaching full maturity [1].

In addition to settling in the pulmonary arteries, the larvae in felines may migrate to ectopic sites, including the central nervous system, abdominal cavities, and even the eyes, leading to serious complications [9].

Adult heartworms generally reach maturity up to 8 months after infection. However, their lifespan is shorter in cats, averaging 2 to 3 years, compared to 5 to 7 years in dogs [1].

This life cycle is illustrated in *Figure 1*, based on the American Heartworm Society guidelines, which highlights the differences in heartworm development between cats and dogs [4].

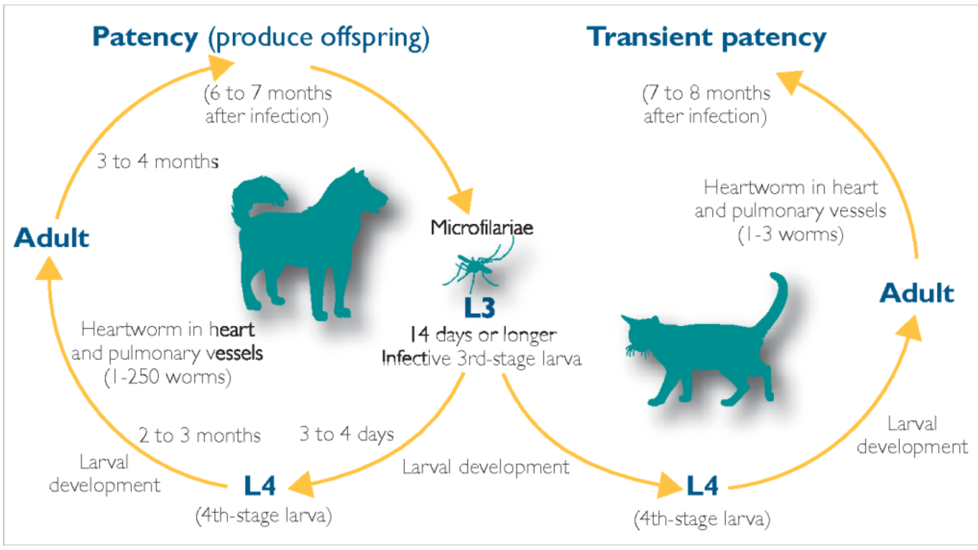

***Figure 1** : Life cycle of Dirofilaria immitis in cats versus dogs (©American Heartworm Society, 2007) [4].*

2.1.3 Vectors and Factors influencing their transmission

The transmission of *Dirofilaria immitis* is dependent on over 70 species of mosquitoes, with significant variation based on geographic regions [1]. In Hungary, *Culex, Aedes*, *Culiseta* and *Anopheles* genera are the vectors the more commonly found [10].

Recent research has highlighted the role of environmental factors in shaping mosquito populations and their capacity to spread heartworm disease. Studies indicate that temperature, humidity, and rainfall significantly affect mosquito breeding and survival rates, which in turn influence the incidence of heartworm infections in both feline and canine populations [11]. Regions characterized by warmer climates often demonstrate heightened mosquito activity, correlating with increased rates of heartworm infections in cats [4].

In addition, the geographical distribution of mosquito species plays a crucial role in the prevalence of heartworm disease. Areas that host a high density of mosquito vectors are more likely to report elevated rates of heartworm infections in cats, underlining the importance of vector monitoring and control strategies to mitigate the risk of heartworm transmission [4], [12].

2.2 GLOBAL PREVALENCE AND REGIONAL VARIANCES

Globally, *Dirofilaria immitis* is primarily a concern in temperate and tropical regions. The disease has gained increasing attention as its prevalence rises in various areas worldwide.

Including all 50 states in the United States. According to the American Heartworm Society, a substantial number of cats exposed to the parasite may develop heartworm disease, with a significant number remaining asymptomatic [4]. In studies conducted by Murillo et al. in 2023 [13], the prevalence of heartworm in cats in the westernmost and southern US states ranged from 3.8% to 20%, varying significantly based on geographic location and local climate conditions. Furthermore, a survey indicated that approximately 15% to 20% of cat owners in endemic regions reported heartworm exposure in their pets, emphasizing the need for regular screening and preventive measures [2].

In Europe, the prevalence of feline heartworm disease has also increased, particularly in southern countries such as Spain, Italy, Portugal and Greece, where it has been demonstrated that the increasing cases in central and northern Europe, are influenced by environmental factors such as climate change, mosquito distribution and by animal movement [4]. A study conducted in Spain found that the antibody seroprevalence of feline heartworm infection was approximately 9.4%, indicating a growing concern for veterinarians and pet owners [14]. Similarly, a survey conducted in Italy revealed a 12% seroprevalence among cats, indicating an increasing occurrence of heartworm disease in the region [15].

The emergence of feline heartworm disease in Northern and Central Europe, including Hungary, has been documented as well, although prevalence rates are generally lower compared to southern regions.

2.3 CLINICAL MANIFESTATIONS IN INFECTED CATS

2.3.1 Pathophysiology of FHW

Feline heartworm disease is a significant clinical concern in cats due to their heightened immune response, which makes even a small number of parasites life-threatening. Although adult heartworms in the pulmonary arteries can lead to localized arteritis, some cats may show no symptoms. However, when clinical signs do develop, they typically occur in two main stages: (1) the arrival of immature heartworms in the pulmonary vasculature, and (2) the death of adult heartworms [4], [5].

1. Arrival of Immature Worms in the Pulmonary Arteries

The first stage of feline heartworm disease occurs when immature adult heartworms arrive in the pulmonary arteries and arterioles, typically 3 to 4 months post-infection. The cat's immune system reacts aggressively to the presence of these immature worms, leading to an acute vascular and parenchymal inflammatory response [4]. This response results in arteritis and damage to the surrounding lung tissue. A significant portion of these immature worms will die during this phase, contributing to the inflammatory response [1], [3]

This acute phase is often mistaken for feline asthma or allergic bronchitis due to overlapping clinical signs such as coughing, wheezing, and dyspnea. However, these symptoms are part of Heartworm-Associated Respiratory Disease (HARD), a syndrome unique to feline heartworm infection [3], [4].

Despite the resolution of clinical signs as the worms mature, histopathological lesions remain in the lung tissue, even in cats that clear the infection. These include occlusive medial hypertrophy of the small pulmonary arterioles and damage to the bronchi, bronchioles and alveoli, as the mechanical presence of the parasites exerts pressure on the endothelium [16], [17]. According to the American Heartworm Society Guidelines [4], the most notable microscopic lesion is the occlusive medial hypertrophy of the small pulmonary arterioles, *Figure 2* illustrates this lesion and its variability in diagnostic states.

Histological changes associated with this phase include goblet cell hyperplasia, eosinophilic infiltration, and bronchiolar lesions characterized by mucus plugs and inflammatory cell infiltration. [17], [18].

Once the pulmonary infection is established, live heartworms appear to modulate immune responses and suppress the inflammation, allowing many cats to tolerate the infection without noticeable clinical signs until the adult worms begin to die [19]. The initial acute phase, therefore, may go unnoticed or misdiagnosed, further complicating the diagnosis of heartworm disease in cats.

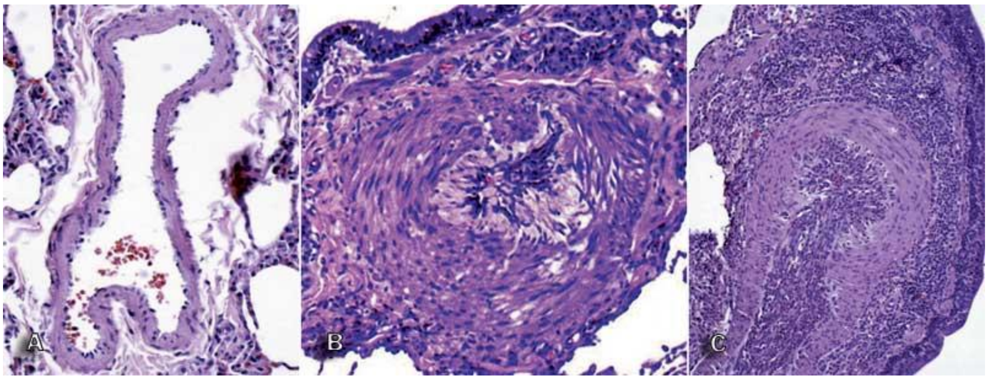

***Figure 2**: Small pulmonary arterioles. A, Adult heartworm and antibody negative. B, Adult heartworm negative and antibody positive. C, Adult heartworm positive [4]*

2. Death of Adult Heartworms

The second stage occurs when the adult heartworms die, either naturally or due to the host's immune system. This phase is particularly dangerous, as the death of the worms often results in a marked pulmonary inflammatory response. As the worms disintegrate, fragments may lodge in the pulmonary arteries, causing pulmonary thromboembolism, which results in the obstruction of blood flow and severe respiratory distress and can cause sudden death, even in single-worm infections [1], [4], [6].

Histologically, eosinophilic pneumonitis is one of the most common parenchymal lesions in this phase, primarily caused by an immune-mediated destruction of microfilariae within the pulmonary vessels, leading to a significant inflammatory reaction [20]. In some cases, eosinophilic granulomatosis occurs, where microfilariae become trapped in the lungs and are surrounded by neutrophils and eosinophils, forming granulomas [19]. As the worms die, the immune system down-regulates its anti-inflammatory response, further exacerbating pulmonary damage and leading to respiratory dysfunction. In some surviving cats, Type II alveolar cell hyperplasia may replace normal Type I cells, resulting in permanent respiratory dysfunction and chronic lung disease, even in the absence of adult worms [16], [19].

In some cases, the chronic immune response and inflammation can lead to pulmonary fibrosis, where scarring of the lung tissue reduces its capacity to exchange oxygen efficiently, resulting in chronic respiratory failure. Even after the worms have died, the persistent inflammatory response can cause permanent lung damage, and many cats continue to experience symptoms such as coughing, wheezing, and exercise intolerance for months or years after the infection [4], [16].

In rare instances, heartworm infections may lead to caval syndrome, a condition where the worms migrate into the right atrium and caudal vena cava, as illustrated in *Figure 3* from the European guidelines from the ABCD on the prevention and management of dirofilariasis in cats [21]. This results in mechanical obstruction of venous return, causing acute cardiovascular collapse. Although caval syndrome is more commonly seen in dogs, it can

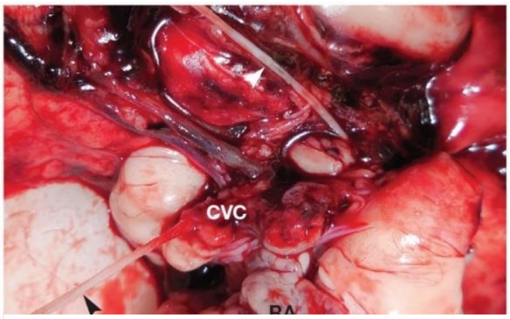

***Figure 3**: Right side of the heart of a cat with heartworm disease (caval syndrome). After removal of the pericardial sac, two adult Dirofilaria immitis nematodes were found (arrowheads), one in the caudal vena cava (CVC). RA = right atrium [24]*

occur in cats with even one or two worms. The worms interfere with the function of the tricuspid valve, leading to tricuspid regurgitation and heart murmurs [4], [8].

In addition to pulmonary and cardiovascular complications, heartworms can also migrate to other organs, including the brain, spinal cord, liver, and eyes. Aberrant migration can lead to diverse clinical signs depending on the site of infection, including neurological deficits, vision problems, and liver dysfunction [1], [17].

Recent studies have also highlighted the role of Wolbachia, an intracellular gram-negative bacterium that lives symbiotically within filarial nematodes, including Dirofilaria immitis. Wolbachia has been shown to contribute to the pathogenesis of heartworm disease by inducing an inflammatory response when released from dying worms [19].

2.3.2 Clinical Signs

The clinical manifestations of feline heartworm disease can vary significantly, depending on the immune response of the individual cat and the stage of the infection. In many cases, cats tolerate the infection well and may exhibit either no clinical signs or only transient symptoms [1], [3], [4]. In a study of 50 naturally infected cats, less than 25% had clinical signs, and the diagnosis was often incidental and 53% that showed symptoms, self-cured within 18–49 months [6]. However, the disease can become severe, particularly when adult worms die, causing pulmonary embolism and triggering acute symptoms[1], [6].

Most cats with clinical heartworm disease present with respiratory signs. These signs can range from persistent tachypnea, intermittent coughing, and dyspnea to increased respiratory effort, which often leads to the misdiagnosis of asthma or allergic bronchitis [1], [3]. Heartworm-Associated Respiratory Disease is now recognized as a key syndrome associated with feline heartworm infections [18].

In addition to respiratory signs, gastrointestinal symptoms such as vomiting, anorexia, and weight loss are frequently reported in cats with heartworm disease. The vomiting is often unrelated to feeding and can be one of the earliest clinical signs [1], [4]. Studies have shown that 24% of cats with heartworm disease presented with vomiting, and 41% showed respiratory signs, with 29% displaying both vomiting and respiratory symptoms [3], [18].

Neurological signs, although less common, can occur when heartworm larvae migrate to ectopic sites, such as the brain or spinal cord. These signs include ataxia, seizures, circling, head tilt, and sudden blindness [1], [19]. In some instances, cats with aberrant larval migration may also display syncope and collapse.

The resulting embolism caused by a dead worm may lead to acute cardiovascular collapse, resulting in sudden death, which occurs in 10% to 20% of heartworm-infected cats without prior significant clinical signs [3]. The primary mechanism behind sudden death is often a massive pulmonary embolus, this triggers an acute immune response to the disintegrating worms, further exacerbating respiratory distress [3], [18]. Cats in this stage may present with acute dyspnea, collapse or sudden death in up to 20% of infected cats [17], [20].

In cases of caval syndrome, it leads to acute signs, including dyspnea, severe lethargy, weakness, and cyanosis from impaired oxygenation [8], [17]. Cats may also exhibit tachycardia, jugular vein distension, hemoglobinuria, and pale mucous membranes due to anemia caused by hemolysis [3].

Apart from the predominant respiratory, gastrointestinal, and neurological signs, feline heartworm disease can also manifest in other ways. Some cats may present with hematological abnormalities, such as anemia, coagulation disorders, and white blood cell abnormalities [19]. In rare cases, cats may develop glomerulonephritis and proteinuria, as heartworm infections can lead to immune complex deposition in the kidneys [6]. Additionally, oncological manifestations, including squamous cell carcinoma and lymphoma, have been reported in heartworm-infected cats, though these associations are less well understood [17].

2.4 DIAGNOSTIC TECHNIQUES AND CHALLENGES

Diagnosing feline heartworm disease poses a significant challenge due to the nature of the infection in cats and the limitations of currently available diagnostic tools. The lack of circulating microfilariae in many feline cases, low circulating antigen levels, the potential for single-sex infections and the relatively low worm burden in cats make it difficult to detect the disease with standard testing methods used in dogs. As such, a comprehensive diagnostic approach using a combination of methods is necessary to improve diagnostic accuracy [22],

[23]. No single test can provide a definitive diagnosis in all cases, so we must consider multiple tests alongside clinical signs and environmental risk factors.

2.4.1. Bloodwork and Additional Testing

Routine bloodwork, including complete blood counts and biochemistry panels, may reveal nonspecific abnormalities such as eosinophilia, anemia, or elevated liver enzymes, However, these findings are not exclusive to heartworm disease and cannot be considered diagnostic on their own [24].

Bronchoalveolar lavage can be used to assess eosinophilia, which is reported to increase in experimentally infected cats, but this finding is not specific to heartworm disease [22]. An increase in eosinophils may indicate various conditions, including allergic bronchitis and other lung parasites, making it necessary to consider these results with other diagnostic information.

2.4.2 Modified Knott Test and Microfilaria Detection

Detecting microfilariae in feline heartworm cases is uncommon, making blood tests for microfilariae largely ineffective as diagnostic tools [17]. Microfilariae are typically only present in dual-sex infections, where both male and female worms are present, and even then, they may only be detectable for one to two months before being cleared by the cat's immune response [1]. Generally, microfilariae can be detected 7 to 9 months post-infection if both sexes are present, but their presence is often transient [4], [25].

Even with the use of concentration techniques such as Knott's test or millipore filters, microfilaremia is detected in fewer than 20% of infected cats [22], [25]. While the presence of microfilariae offers 100% specificity for diagnosing *Dirofilaria immitis* infection, it is important to recognize that other filarid species, such as Dirofilaria repens, may also cause microfilaremia in cats, further complicating the diagnostic process [17].

2.4.3 Serology

Antigen Testing:

Antigen tests, considered as the most reliable method for diagnosing heartworm disease in dogs, detect specific proteins produced by adult female heartworms. However, the application of these tests in cats is more limited due to the unique characteristics of feline infections. These tests typically utilize enzyme-linked immunosorbent assay (ELISA) technology to identify proteins secreted primarily by the reproductive tract of female worms. These antigens become detectable in the bloodstream approximately 5.5 to 8 months post-infection, which corresponds to the maturation of larvae into adult worms [26]. While antigen tests have a high specificity, ranging from 96% to 99%, their sensitivity in cats can be significantly lower, often dropping to around 50% in naturally infected cases. This reduced sensitivity is particularly problematic in cases of low worm burden or infections that involve only male worms, as antigen tests primarily detect female-specific proteins. Additionally, infections with immature female worms may go undetected because antigen production does not occur until the worms reach maturity, which can take several months [24], [25].

False-negative results are a significant concern with antigen testing, as they can lead to misdiagnosis, causing veterinarians to overlook the presence of heartworm disease. In some cases, antigen detection may be further hindered by immune complexes that interfere with the test results. Research suggests that heating serum samples to 104°C for 10 minutes may break down these complexes and enhance test sensitivity [27]. However, this practice is not widely recommended, as it may compromise the accuracy of combination tests that also detect antibodies.

Antibody Testing:

Antibody tests are a valuable tool in diagnosing feline heartworm disease, as they detect antibodies produced by the cat's immune system in response to exposure to heartworm larvae, particularly during the L4 stage [4]. These tests can detect antibodies as early as 2 months after infection, indicating that the cat has been exposed to the parasite. However, they do not confirm the presence of adult worms [28]. While early studies showed that antibody tests could achieve sensitivities as high as 98% in experimentally infected cats [29], necropsy studies of naturally infected cats have reported variable sensitivities, ranging from 32% to 89%. [24], [30]. This variability can be attributed to factors such as the population tested. Experimentally infected cats often receive a higher dose of larvae, leading to a more robust immune response, as well as the timing of the test in relation to the infection. Antibody levels may decrease over time, potentially leading to false-negative results.

A positive antibody test may indicate a current infection with adult worms, a recently cleared infection, an infection caused by immature larvae, or past exposure to the parasite [22]. However, cross-reactivity with antibodies produced in response to other helminths or parasites is also possible, necessitating further confirmation through additional tests or morphological analysis.

In regions where heartworm disease is endemic, antibody testing remains particularly useful for assessing exposure risk and raising clinical suspicion. To improve diagnostic accuracy, combining antigen and antibody tests is recommended, as studies have shown that using both methods together can improve sensitivity and specificity, potentially reaching as high as 100% and 99.4%, respectively. However, while these tests can provide valuable information for clinical decision-making, they should not be relied upon exclusively for a definitive diagnosis.

2.4.4 Thoracic Radiography

Thoracic radiography is another valuable diagnostic tool in assessing heartworm infection in cats, particularly for evaluating pulmonary damage and monitoring the progression of the disease [22]. Heartworms can cause significant inflammation and scarring in the lungs and pulmonary arteries, often leading to characteristic radiographic findings. One of the most common signs observed in heartworm-positive cats is a diffuse bronchointerstitial pattern in the pulmonary parenchyma. This pattern is illustrated in *Figure 4*, which shows a thoracic radiograph of a 12-year-old cat with heartworm infection, as reported in the first clinical report of feline heartworm infection in Romania by D. Pană et al. [31]. Radiographs may show focal or diffuse areas of increased opacity in the lungs, which can represent inflammation, fibrosis, or even pulmonary hyperinflation.

In some cases, right ventricular enlargement may be evident, particularly in cases where pulmonary hypertension is present. This occurs as a result of the increased workload on the right side of the heart due to obstruction of pulmonary blood flow by adult heartworms within the pulmonary arteries [32]. These pulmonary and cardiac changes are associated with HARD, that mimics other respiratory conditions such as asthma, allergic bronchitis, or aelurostrongylosis [22].

Another important radiographic feature in cats with heartworm disease is pulmonary artery enlargement, which occurs due to the presence of adult heartworms in the pulmonary arteries, this may cause the arteries to become enlarged or tortuous, a change that is typically most pronounced in the right side of the pulmonary arteries, particularly seen in ventrodorsal or dorsoventral radiographic views, as illustrated in *Figure 5*, based on the same case report of feline heartworm infection from Romania [31], [33]. A key metric in identifying heartworm disease in cats is the ratio of the width of the right pulmonary artery to the width of rib 9 in the DV or VD view. If the right pulmonary artery is greater than 1.6 times the width of rib 9 at the caudal border of the rib, this is strongly indicative of heartworm disease [32], [34].

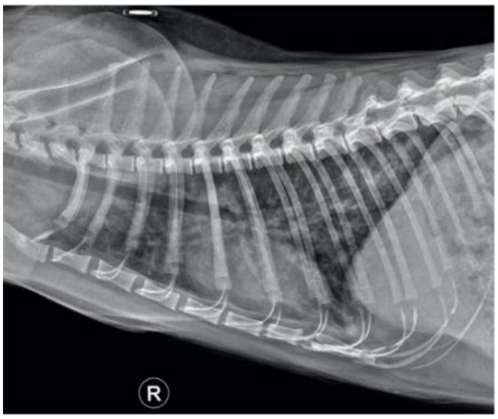

Figure 4*: Thoracic radiograph showing a diffuse bronchointerstitial pattern in a 12-year old cat with heartworm infection (lateral view) [36].*

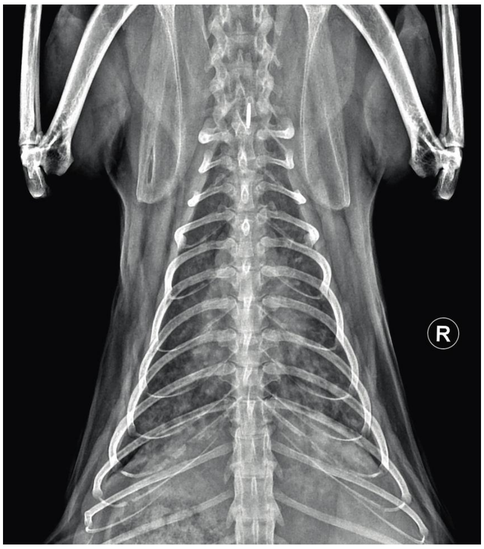

Figure 5*: Thoracic radiograph showing enlarged caudal lobar pulmonary arteries in a 12-year-old cat with heartworm infection (dorsoventral view) [36].*

Another measurement, the Vertebral Heart Score, can be used to assess heart size on lateral radiographs in heartworm-infected cats. Studies indicate that the heart size of affected cats is significantly larger than in healthy cats [32]. However, the enlargement of the heart is not as prominent or as consistent a finding as it is in dogs with heartworm disease.

Additionally, rare complications like pleural effusion due to hydrothorax or chylothorax, as well as evidence of pulmonary thromboembolism, may also be visible on radiographs in severe cases of infection [22].

Despite these key findings, radiographic abnormalities in cats with heartworm disease are less consistent than in dogs, and the absence of radiographic abnormalities does not exclude the possibility of infection [34]. Some heartworm-infected cats may exhibit normal radiographs, especially in early or less severe stages of infection.

2.4.5 Echocardiography

Echocardiography is one of the most definitive antemortem methods for diagnosing heartworm infection in cats. It allows for direct visualization of the worms, which appear as hyperechoic, double-lined structures in the pulmonary arteries or heart chambers, as illustrated in *Figure 6*, based on the case report from Romania, showing heartworms as short, segmented, strongly echogenic parallel lines in the right pulmonary artery [31], [35]. In addition to confirming the presence of worms, echocardiography provides critical information about heart and lung damage, which helps guide treatment decisions [22]. However, its sensitivity can be affected by the worm burden. In cases of low worm numbers, worms may not always be visible, making echocardiography less effective in mild infections [35].

In one retrospective study, echocardiography detected heartworms in 17 out of 43 cats, with worms found mainly in the pulmonary arteries and occasionally in the right ventricle, right atrium, and caudal vena cava [35]. In some cases, echocardiography was the only diagnostic method that successfully identified the infection, especially when antigen tests were negative. False positives are rare but can occur due to linear densities in the pulmonary artery bifurcation, which may mimic heartworms. These densities are presumed to be reflections from the artery walls, though their exact cause is not well understood [35].

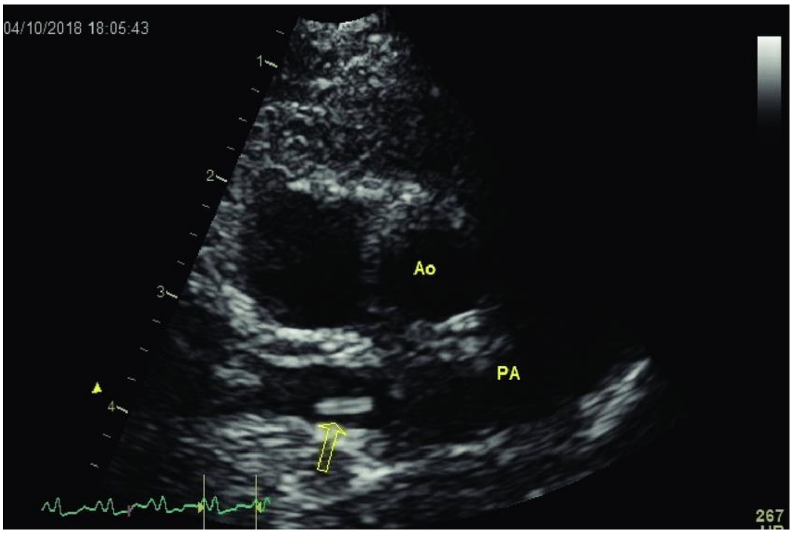

Figure 6: Echocardiogram showing heartworms, seen as short, segmented, strongly echogenic parallel lines in the right pulmonary artery (arrow) of a 12-year naturally infected cat (Ao: aorta; PA: pulmonary artery) (right parasternal short axis view at the heart's base) [34]

2.4.6 Necropsy

Post-mortem examination is the most definitive diagnostic method for confirming heartworm infection. It allows for direct visualization of adult heartworms, providing conclusive evidence of infection. However, necropsy is only applicable in fatal cases, which significantly limits its usefulness as a routine diagnostic tool in living cats [22], [24].

Ectopic infections are more common in cats and may be overlooked during routine necropsy [24]. Additionally, precardiac infections, in which the larvae are still in their pre-adult stages, can cause clinical signs but may not be detected during necropsy due to the absence of mature worms [32].

Ultimately, while the integration of multiple diagnostic methods can enhance accuracy, the cost of comprehensive testing can be prohibitive for some pet owners. Even with thorough diagnostic evaluations, some infections may still go undetected.

2.5 TREATMENT STRATEGIES

Treating FHW is a complex and delicate process due to the unique physiology of cats and the high risks associated with adulticidal therapies. Unlike dogs, where heartworm treatment often focuses on killing adult worms, this approach is rarely used in cats due to the potential for life-threatening complications such as pulmonary embolism. Instead, the management of FHW in cats typically revolves around addressing the clinical symptoms caused by the disease and controlling secondary infections or complications. Therefore, the strategy generally includes symptom management: reducing inflammation, controlling the body's immune response, preventive care, and, in rare cases, surgical intervention.

2.5.1 Pharmacological Approaches

The cornerstone of managing symptoms associated with feline heartworm disease is the use of corticosteroids, with prednisolone being the most prescribed. Corticosteroids work by suppressing the immune response to parasites and mitigating the resulting inflammation, thereby improving respiratory function and reducing lung damage.

Prednisolone is typically initiated at a dosage of 2 mg/kg of body weight per day, gradually decreasing to 0.5 mg/kg every other day over two weeks, followed by discontinuation after an additional two weeks. The effects of this treatment should be reassessed based on clinical response and thoracic radiography. This treatment may be repeated in cats that exhibit recurrent clinical signs [4].

In advanced cases of FHW, supportive care becomes essential to manage severe respiratory distress or cardiovascular compromise. Oxygen therapy may be required for cats with significant pulmonary disease, while fluid therapy can help maintain hydration and address any electrolyte imbalances resulting from chronic vomiting or diarrhea. Bronchodilators can also be prescribed, these medications are particularly beneficial for cats displaying symptoms of wheezing or labored breathing, facilitating better airflow in the lungs.

A critical aspect of treating heartworm infection involves addressing the bacterial symbiont, Wolbachia. Research in dogs has demonstrated that using doxycycline to reduce Wolbachia populations disrupts heartworm embryogenesis and effectively kills larvae [36]. However, prolonged administration may lead to side effects such as gastrointestinal issues [37]. In cats, studies are ongoing to evaluate whether suppressing Wolbachia with doxycycline prior to adulticide therapy provides clinical benefits. The American Heartworm Society notes that the utility of this treatment approach for cats is still under investigation [4].

In stable cats that continue to show clinical signs unresponsive to empirical corticosteroid therapy, adulticide treatment may be considered a last resort. However, there is limited clinical experience with melarsomine dihydrochloride in cats, and its use is typically discouraged because early data indicates toxicity at doses as low as 3.5 mg/kg [38], [39].

2.5.2 Surgical Approaches

While surgical treatment for FHW is rare, it may be considered for cats with a high burden of adult heartworms, particularly when these worms are causing life-threatening blockages in the pulmonary arteries or right heart chambers. Although surgery can be life-saving, it carries significant risks, especially given that anesthesia poses dangers for cats with compromised pulmonary and cardiovascular function. Additionally, the surgical procedure can lead to pulmonary thromboembolism, where dislodged worms or clots obstruct smaller blood vessels.

Surgical techniques can involve using brush strings, basket catheters, or loop snares introduced via right jugular venotomy. Alternatively, after a left thoracotomy, alligator forceps may be inserted through a purse-string incision in the right ventricle [40], [41]. Before attempting surgical approach, it is critical to identify the location of heartworms using ultrasonography to ensure they can be reached with the instruments [41]. When accessing from the right jugular vein, it is important that the worms are present in the cavae or right atrium, as achieving access to the right ventricle can be challenging [4].

Both atria, ventricles, and the main pulmonary artery can be accessed through a ventriculotomy incision with straight alligator forceps [41]. Surgery is particularly indicated in cases that develop caval syndrome [4]. Care must be taken to remove the worms intact; partial or complete transection of a worm can lead to acute circulatory collapse and death [42].

2.6 PREVENTIVE MEASURES

2.6.1 Pharmacological Measures

Awareness among veterinarians regarding the importance of heartworm prevention has significantly increased, leading to the recommendation of preventive medications, especially during peak transmission seasons. Heartworm preventives are the most crucial tool in managing feline heartworm disease. These medications target and kill the larval stages of *Dirofilaria immitis* before they can mature into adult worms.

Preventive medications are available in both oral and topical formulations and are typically administered year-round. This year-round administration is vital, as mosquitoes can remain active even in colder months in certain regions. It is recommended to start administering heartworm preventives to kittens at 8 weeks of age and to continue this practice for all cats in endemic areas throughout the heartworm transmission season [4]. The individual minimum monthly prophylactic doses for various preventive medications are as follows:

Ivermectin: 24 µg/kg orally [43]

Milbemycin oxime: 2.0 mg/kg orally (in combination with praziquantel) [44]

Moxidectin: 1.0 mg/kg topically or spot-on (in combination with imidacloprid) [45]

Selamectin: 6.0 mg/kg topically or spot-on (may be in combination with sarolaner) [46]

Eprinomectin: 0.48 mg/kg topically or spot-on (in combination with praziquantel and (S)-methoprene and fipronil) [47]

The administration of these drugs is not contraindicated by the presence of antibodies or antigens in cats. Although testing cats before starting heartworm preventives is recommended, it is generally considered less critical than it is for dogs, due to the unique response of cats to heartworm infections [4].

2.6.2 Non-Pharmacological Measures

In addition to pharmacological approaches, implementing non-pharmacological measures is important for minimizing the risk of heartworm transmission. Since mosquitoes are the primary vectors for heartworm, controlling their exposure can significantly reduce the risk of infection. Effective vector control strategies involve keeping cats indoors to limit their exposure to mosquitoes, although it is important to note that indoor cats are still at risk if mosquitoes enter the home environment. Furthermore, reducing mosquito populations can be achieved by eliminating standing water where mosquitoes breed, using insect repellents, and installing screens on doors and windows to protect cats from bites. It is crucial for cat owners to take proactive steps to keep mosquitoes out of the home environment, especially in regions with a high risk of heartworm transmission [4].

By combining both pharmacological and non-pharmacological strategies, cat owners can effectively reduce the risk of heartworm infections and safeguard their feline companions against this potentially life-threatening disease.

OBJECTIVES

This study employed a cross-sectional design to examine the prevalence of feline heartworm disease in domestic cats in Budapest, presenting with respiratory symptoms. The objective was to detect heartworm antibodies, through the use of antibody tests to identify immune responses indicative of prior exposure to *Dirofilaria immitis* larvae.

By focusing on cats with respiratory symptoms, a secondary objective was to evaluate whether heartworm infection could be linked to these clinical signs. The research aimed to correlate clinical presentations and endoscopic results with serological findings, thereby assessing whether heartworm-associated respiratory disease may be underdiagnosed in this population. Additionally, the study sought to explore possible environmental and host-related risk factors, such as living environment and prophylactic measures, that could influence the prevalence of FHW.

MATERIALS AND METHODS

The sample population included five domestic cats of varying ages, sexes, and living environments, brought to the university clinic in Budapest for veterinary evaluations, between 22nd August 2023 and 20th February 2024. All cats exhibited respiratory symptoms such as coughing and tachypnea, which are often associated with HARD. The selection of cats with respiratory symptoms increased the likelihood of identifying positive cases, as respiratory issues are a hallmark of FHW. All procedures were carried out with the consent of the cats' owners.

Blood samples were collected from the five cats using standard venipuncture techniques, including needles, syringes, and collection tubes. The blood was then processed to detect antibodies against *Dirofilaria immitis* using commercially available FeliCheck-3 tests. This diagnostic method detects the presence of antibodies produced by the immune system in response to prior exposure to heartworm larvae, allowing for the identification of immune responses even when the adult worms are not present. The antibody testing was conducted in a controlled laboratory setting, and results were recorded meticulously for each case.

Endoscopy was also performed on each cat to visually assess the respiratory tract for any signs of heartworm infection or other abnormalities. The endoscopic examination allowed for direct visualization of the trachea and bronchi, providing detailed information on the degree of bronchial inflammation and helping to confirm or rule out other potential causes of respiratory distress, such as chronic bronchitis. The findings from the endoscopic evaluations were compared with the antibody test results to provide a comprehensive picture of each cat's health status.

All data, including clinical observations, antibody test results, and endoscopic findings, were compiled into a structured dataset. Descriptive statistics were employed to summarize the findings. This included an analysis of the health conditions and respiratory symptoms of the cats, the test results, and the extent of bronchial inflammation observed during endoscopy. The study did not employ inferential statistics due to the limited sample size, but instead focused on descriptive analysis to provide insights into the prevalence and potential causes of respiratory symptoms in the cats tested.

The final analysis involved evaluating whether heartworm infection could be confirmed as the underlying cause of the respiratory symptoms in any of the cats. The comparison between antibody test results and endoscopic findings helped determine whether feline heartworm disease could be implicated in the observed clinical signs, or if other causes such as chronic bronchitis were more likely. This study aimed to contribute to the understanding of feline heartworm prevalence and explore the diagnostic challenges posed by FHW in cats.

RESULTS

In this study, five cats were tested for heartworm disease. *Table 1* shows a breakdown of the cases.

***Table 1**: Clinical Characteristics and Heartworm Test Results of the Five Cats in the Study.*

Age	*Sex*	*Breed*	*Indoor/ outdoor*	*Symptoms*	*Prophylaxis*	*Antibody Test*	*Endoscopy*
12 years old	Male	DSH	Outdoor	Coughing	No	Negative	Chronic bronchitis
2 yrs	Male	DSH	Indoor	Coughing	No	Negative	Chronic bronchitis
1 yr	Male	DSH	Indoor	Tachypnea	No	Negative	Subacute-acute bronchitis
5 yrs	Female	DSH	Outdoor	Coughing	No	Negative	Chronic bronchitis
2 yrs	Female	DSH	Outdoor	Coughing	No	Negative	Chronic bronchitis

The sample consisted of 5 cats, with an average age of 4.4 years. Most of the cats (60%) were outdoor cats, and none had received heartworm prophylaxis. All five cats exhibited respiratory symptoms such as coughing or tachypnea, which are commonly associated with HARD, and the antibody tests were negative for all cats. Endoscopy revealed chronic bronchitis in 4 of the 5 cats and subacute-acute bronchitis in the fifth cat. The results suggest that despite the respiratory symptoms, none of the cats had detectable immune response to heartworm infection at the time of testing based on antibody testing.

The uniformly negative results present an opportunity to explore potential reasons for this outcome by considering various risk factors, limitations of diagnostic tests, and comparisons with both canine and feline heartworm studies in Hungary and other European countries.

DISCUSSION

Research on feline heartworm disease in Hungary remains extremely limited, particularly when compared to studies conducted on canine heartworm disease. In contrast, European countries such as Italy, Portugal and Spain have contributed significantly to the understanding of feline heartworm prevalence, offering insights that can be extrapolated to the Hungarian context. Studies on heartworm prevalence in dogs have established the presence and spread of *Dirofilaria immitis* and *Dirofilaria repens* in Hungary [48]. However, our understanding of the epidemiological profile of FHW in Hungary, particularly in urban areas like Budapest, is still lacking. The absence of extensive feline data within Hungary hinders our ability to fully contextualize the negative results obtained in this study. In countries like Romania, where the prevalence of heartworm disease has been well studied, there is evidence of heartworm infections in cats, although at lower rates than in dogs. This raises questions about whether the negative results in our study are reflective of a genuinely low prevalence of FHW in Budapest or whether other factors, such as the sensitivity of the diagnostic tools or timing of testing, may have contributed to the results. This discussion will focus on interpreting the negative results of our study on the cats tested for FHW, while contextualizing our findings within broader European and canine heartworm studies.

In this study, five cats were selected for antibody testing based on the presence of respiratory symptoms such as coughing and tachypnea, which are commonly associated with HARD. Despite these clinical signs, none of the cats tested positive for heartworm antibodies. This outcome raises several important questions regarding the prevalence of feline heartworm in Hungary and how we should interpret these negative results.

One of the critical factors influencing the prevalence of heartworm infections is the seasonal activity of mosquitoes, which are the primary vectors for *Dirofilaria immitis*. Mosquitoes are generally less active during the colder months in Hungary, which could explain the absence of positive results from the 3 tests out of 5 conducted during the cold season, between January 18 and February 20 2024. Studies have shown that heartworm transmission is highest during the summer months when temperatures consistently exceed 14°C, which is necessary for the maturation of heartworm larvae within the mosquito [1].

In European studies, the prevalence of feline heartworm disease is generally lower than in dogs, ranging between 2% and 5% in most regions [15]. In Spain, the study by Montoya-Alonso et al. confirmed that feline heartworm is present wherever canine heartworm is endemic, with antibody seroprevalence rates of up to 19% in some regions, such as the Canary Islands [14]. However, in more temperate regions with lower mosquito activity, the prevalence was significantly lower. The geographical variation observed in Spain is likely applicable to Hungary, where seasonal temperature fluctuations and the urban environment of Budapest may contribute to a lower risk of feline heartworm infection.

In Italy, a study demonstrated that *Aedes albopictus*, a mosquito species known for spreading heartworm, is expanding its range due to climate change, potentially increasing the risk of heartworm transmission in both dogs and cats [15]. Warmer climates in southern Europe, such as those found in Spain, Portugal and Italy, are more conducive to mosquito populations, resulting in higher rates of heartworm infection in both cats and dogs.

Eastern European countries such as Romania, Bulgaria, and Hungary experience more temperate climates, with colder winters that limit mosquito activity to the summer months. As a result, heartworm prevalence in these countries tends to be lower. Studies from Romania report a heartworm prevalence of 12% in dogs, particularly in regions near the Danube Delta, but there is limited data on feline heartworm prevalence [2]. Bulgaria and Croatia, with similar temperate climates, also report lower heartworm prevalence due to colder winters that limit mosquito activity. These findings are consistent with the results in Hungary, where colder winters may contribute to the low prevalence of feline heartworm infections [2]. The study done by Farkas et al. also emphasized the importance of climatic conditions in influencing heartworm transmission. Warmer temperatures, particularly in the summer, accelerate the development of infective L3 larvae within mosquitoes, increasing the risk of heartworm transmission in regions such as those near the Danube and Tisza rivers [48].

The urban environment of Budapest may also play a role in the low prevalence of heartworm infections in domestic cats. Cats living in densely populated cities may have less exposure to mosquitoes compared to cats in rural areas where breeding grounds for mosquitoes are more prevalent. The 2020 study by Farkas et al. indicated a higher prevalence of heartworm in outdoor dogs compared to indoor dogs, reflecting their increased exposure to mosquitoes [48]. Although some cats in the study were outdoor cats, their exposure to heartworm-transmitting mosquitoes would still be limited in an urban environment, where stagnant water and other mosquito breeding sites are less common. This contrasts with studies conducted in rural or suburban settings, where mosquitoes are more abundant, and therefore, heartworm infections are more likely. The urban nature of the study setting in Budapest may have contributed to the negative results, as it limits the cats' exposure to the vector.

When comparing these findings with the study in Spain, we see that heartworm prevalence was also lower in urban regions compared to rural areas. However, seropositive samples were still observed in indoor cats, with rates ranging from 15.3% in outdoor cats, 12.9% in indoor/outdoor cats, and 5.6% in indoor cats, demonstrating that even indoor cats can be exposed to mosquitoes [14]. This highlights the need for prophylactic measures in all cats, regardless of their habitat. In Hungary, the absence of similar studies makes it difficult to assess how much urbanization may impact heartworm prevalence in cats.

Studies in other European countries support this observation. In Italy, a study found that *Dirofilaria immitis* transmission is more prominent in rural and suburban areas, with urban environments showing lower transmission rates due to fewer mosquitoes [15]. Similarly, a study in Spain revealed that urban cats have lower heartworm seroprevalence than those living in rural or coastal regions, where environmental factors favor mosquito breeding and higher infection rates [14].

Studies on canine heartworm disease in Hungary have reported relatively high prevalence rates, found that 11.3% of dogs tested in Hungary were positive for heartworm, with hotspots identified primarily in rural areas near water bodies, which have significant mosquito breeding sites [48]. The study is shedding light on the regional distribution, climatic factors, and host-related characteristics that influence the spread of *Dirofilaria immitis*. The canine prevalence showed a strong correlation with mosquito activity and climatic conditions, with dogs residing in more mosquito-dense areas displaying higher infection rates. In contrast, no cats in this study tested positive, highlighting the potential differences in exposure and susceptibility between dogs and cats. However, it is important to note that canine studies typically involve larger sample sizes and often include dogs from rural areas with higher mosquito exposure. The absence of a similar, comprehensive study on feline heartworm prevalence in Hungary limits our ability to make direct comparisons between species.

This data can be instrumental when comparing canine heartworm prevalence to potential feline infection, applying the commonly cited 10% ratio of feline-to-canine prevalence (based on previous research [4]) would suggest that feline heartworm prevalence in Hungary should be around 1-1.5%. However, given the small sample size of five cats in this study, statistical probabilities show that the likelihood of detecting a positive case would be minimal. Indeed, the chances of all five cats testing negative (assuming a 1% prevalence rate) would be around 95.1%. Therefore, the negative results in this study align with expectations given the small sample size and low overall prevalence.

Another crucial factor is the immune response of cats, which differs significantly from that of dogs. Cats are not the primary hosts for *Dirofilaria immitis*, and their immune systems often eliminate the larvae before they can develop into adult worms and often prevent the production of circulating microfilaria [22]. Even if a cat was exposed to heartworm larvae, the infection may not have progressed far enough to produce detectable antibodies. Cats also tend to harbor fewer adult worms than dogs, with many infections consisting of only one or two worms, further complicating the detection of the disease [1]. In this study, it is possible that the cats' immune systems cleared the infection before antibody production could occur, contributing to the negative results.

The limitations of the antibody test used in this study must also be addressed. As seen previously, while antibody tests are valuable to detect past exposure to heartworm larvae, they do not necessarily confirm an active infection. Furthermore, cats with low worm burdens may not produce detectable levels of antibodies, leading to false-negative results. Antibody levels can also decrease over time, particularly if the infection has been cleared, making it difficult to detect previous exposure [22]. Additionally, the sensitivity of the antibody test in detecting *Dirofilaria immitis* in cats can vary, depending on the stage of infection and the number of worms present [24]. This limitation suggests that while the cats tested negative for antibodies, it does not definitively rule out the possibility of previous heartworm infection, especially given the clinical signs exhibited by all the cats.

Antigen tests, which detect proteins produced by adult female heartworms, are considered more definitive for diagnosing heartworm infections in dogs. However, antigen tests are less reliable in cats due to their typically low worm burdens and potential single-sex infections. In Spain, Montoya-Alonso found that while the mean antibody seroprevalence in cats was relatively high at 9.4%, antigen test results were significantly lower at 0.5% [14]. This highlights the difficulty of diagnosing feline heartworm infections and suggests that future studies in Hungary should incorporate a multimodal diagnostic approach, which is crucial when diagnosing feline heartworm disease. Studies have demonstrated that combining different diagnostic methods can increase sensitivity and specificity, potentially reaching 100% sensitivity when both antigen and antibody tests are used together [2]. Radiography and echocardiography should be employed alongside antibody and antigen testing to improve diagnostic accuracy.

The small sample size of five cats is another significant limitation of this study. Although the cats were selected based on respiratory symptoms, which are commonly associated with heartworm disease, the sample size limits the statistical power of the study and reduces the ability to generalize the findings to the broader feline population in Hungary. A larger sample size would be necessary to draw more robust conclusions about the prevalence of heartworm disease in domestic cats in the city. The absence of other feline studies on heartworm prevalence in Hungary further complicates efforts to compare our results with broader national trends.

CONCLUSION

The negative results in this study can be attributed to several factors, including the timing of the study in relation to mosquito activity, the urban setting of Budapest, the immune response in cats, and the limitations of the antibody test used. Additionally, the small sample size and the lack of extensive research on feline heartworm disease in Hungary further limit the ability to draw definitive conclusions. Future studies with larger sample sizes, conducted during peak mosquito season, and employing a combination of diagnostic tests, such as antigen testing and imaging, are necessary to better understand the prevalence and impact of feline heartworm disease in Hungary. Longitudinal studies to monitor feline populations over time could also be interesting. Such studies can provide insight into how environmental changes, vector populations, and preventive measures impact the prevalence of heartworm disease. Furthermore, establishing a baseline for feline heartworm prevalence in Hungary would provide valuable insights into the risk factors and transmission dynamics of this disease in domestic cats.

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