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A CASE REPORT AND SYSTEMATIC REVIEW OF HUMAN DIROFILARIASIS: INSIGHTS INTO GLOBAL DISTRIBUTION, RISK FACTORS, CLINICAL PATTERNS, DIAGNOSTIC TECHNIQUES AND THERAPEUTIC STRATEGIES

General Surgery

Dr. Joseph Francis MBBS, MS, Associate Professor, Department of General Surgery, Travancore Medical College, Kollam, Kerala.

Dr. Linta Maria David MBBS, Junior Resident, Department of General Surgery, Travancore Medical College, Kollam, Kerala.

Dr. Annie Joseph MBBS, Junior Resident, Department of General medicine, Jubilee Mission Medical College, Thrissur, Kerala, India

ABSTRACT

Background: Human infection with dirofilariasis is extremely uncommon and normally presents as benign, self-limiting infections. Subcutaneous nodules or, less frequently, pulmonary lesions or ocular infections are the most common outcomes of human infections. **Method:** A systematic review was carried out by searching, screening, and analysing a total of 145 published clinical cases of human dirofilariasis worldwide according to PRISMA guidelines. **Result:** D. repens is the primary cause of human dirofilariasis, according to data extracted from a subset of publications that included 145 case cases. Dirofilaria repens was also identified as the causal organism in a case of dirofilariasis that the investigators successfully treated and documented herein as case report. Most patients presented with subcutaneous nodules. Surgery is generally proceeded with even if noninvasive techniques are employed during the preoperative management. The molecular approach is still the most accurate method for diagnosing at the species level, despite its limited use to date. **Discussion:** Tardiness of the patients in seeking assistance as well as frequency of error in clinical suspicion done by doctors are very decisive, concerning management. Development of cost-effective, rapid diagnostic kits like species-specific serological or molecular assays, implementation of training programs to improve the availability of histopathological expertise in endemic areas, increased awareness in endemic regions with further studies on diagnostic methods and possible medical therapies may be of immense help in timely diagnosis and management of this disease

KEYWORDS

Human Dirofilariasis, Dirofilaria infection, Dirofilaria repens, Dirofilaria immitis

INTRODUCTION

Dirofilariasis is a zoonotic disease caused by Dirofilaria species, mainly Dirofilaria immitis and Dirofilaria repens, which are parasites primarily infecting canines, felines and other animal hosts. Human infection with dirofilariasis is very rare and typically manifests with benign, self-limiting infections. Most human infections result in subcutaneous nodules or, less commonly pulmonary lesions or ocular infections. The proliferation of vector mosquitoes has led to a rise in dirofilaria infections among humans in regions previously regarded as rare. This study entails a case report of this rare disease managed by the authors and a systematic review therein has been designed to consolidate and synthesize the existing knowledge regarding human dirofilariasis, encompassing the disease's manifestation through clinical characteristics, diagnostic methodologies and current treatment approaches.

Case Report

A 21-year-old male patient presented to the OPD with complaints of swelling over the left side of front of neck since 3 weeks.

Fig 1: Presenting As Swelling In The Left Side Of Neck

Pre operative USG Neck taken showed elongated parasite inside the cavity. Patient was posted for excision after routine evaluation. Excision of cavity done under GA and 15cm long live worm was extracted.

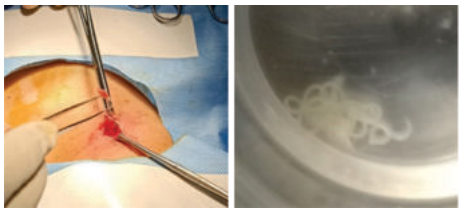


Fig 2: Showing Peroperative Extraction Of The Live Worm

Specimen of live worm was sent for bacteriological examination in normal saline and was identified as female Dirofilariasis repens.

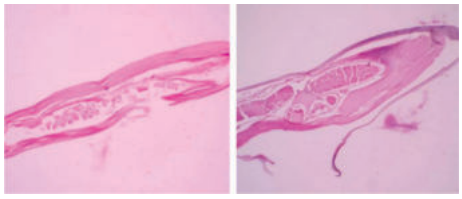


Fig 3: Histopathology Sections Of Extracted Worm Identified As Female Dirofilaria With The Presence Of Polymyarian Musculature, External Cuticular Ridges And Paired Reproductive Tubes

Post-operative period was uneventful. Wound care and anti-parasitic treatment with Ivermectol was given and patient was asymptomatic up to 2 years postop.

Objectives

This systematic study aims at analyzing the existing literature on human dirofilariasis cases in order to establish a more precise portrayal of the disease, in terms of geographic distribution, risk factors, clinical presentations, diagnostic techniques, and therapeutic approaches.

METHODS

Search Strategy

A comprehensive review was conducted using the major medical

databases, which included articles from Pubmed, Scopus and Embase since 2000 up to October 2024. Literature searching for the comprehensive review was conducted systematically and rigorously, making sure that only relevant and high quality research was considered. This was especially to answer the research question- what clinical, epidemiologic and diagnostic characteristics of human dirofilariasis have been reported in the published literature. Search terms incorporated were human dirofilariasis, Dirofilaria infection, Dirofilaria repens and Dirofilaria immitis. The initial search yielded a total of 320 studies. After screening for duplicates, 275 studies were reviewed for screening.

Eligibility Criteria

Inclusion Criteria

Studies included in the review had to satisfy the following criteria:

- **Study Type:** articles from peer-reviewed journals, case reports, case series, and observational studies.
- **Population:** Studies involving human cases of dirofilariasis, regardless of age, gender, or geographical location.
- **Language:** Studies published in English, as the majority of the literature on human dirofilariasis is available in this language.
- **Timeframe:** Studies published from the year 2000 to 2024, as this period saw significant advancements in diagnostic methods and global reporting on dirofilariasis.
- **Relevance:** Studies reporting on the clinical features, diagnostic methods, epidemiology, and treatment of human dirofilariasis.
- **Species:** Studies focusing on human infections caused by Dirofilaria species, particularly Dirofilaria immitis and Dirofilaria repens.

Exclusion Criteria

Studies were excluded if they:

- Were not peer-reviewed (e.g., conference abstracts, opinions, or non-original research articles).
- Focused on veterinary cases or animal models of dirofilariasis.
- Failed to describe clinical presentations, diagnostic methods, therapeutic interventions, or epidemiological data in detail.
- Published before 2000 or after 2024 or fall out of the scope of the review.

Study Selection Process

1. **Title and Abstract Screening:** In the initial screening, relevance of the studies were assessed based on their titles and abstracts by two independent reviewers who were blinded to each other's decisions to minimize bias. Those studies that were obviously irrelevant or did not meet the inclusion criteria were eliminated. This process resulted in a filtered set of studies that were eligible for full-text review. In total, 77 studies passed this initial stage and were considered for further evaluation.
2. **Full-Text Review:** 61 selected articles underwent full-text review by two independent reviewers who carefully read and assessed each article for its relevance to the research question and to ensure it satisfied the inclusion criteria. Any disagreements between the two reviewers regarding the inclusion or exclusion of a study were resolved through discussion or by involving a third reviewer. After careful evaluation, a total of 34 studies were included in the final review. These studies were deemed to meet the inclusion criteria and contributed valuable data on the clinical, diagnostic, and epidemiological aspects of human dirofilariasis.

Data Extraction

Data were extracted on:

- Geographic distribution
- Demographic characteristics
- Clinical presentation (e.g., subcutaneous, ocular, or pulmonary infections)
- Diagnostic methods (imaging, serology, histopathology)
- Treatment modalities and outcomes

Quality Assessment

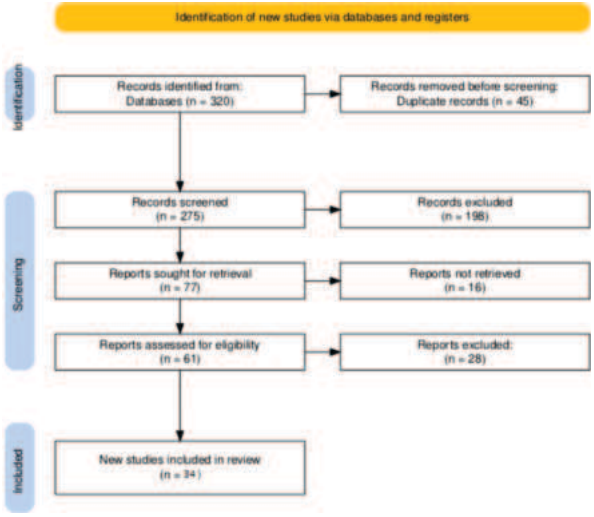
Studies were evaluated for risk of bias using the Cochrane Risk of Bias Tool which yielded overall low to moderate risk of bias over 4 risk domains. The GRADE (Grading of Recommendations, Assessment, Development, and Evaluation) framework was applied to rate evidence quality across four domains: Study Design and Risk of Bias, Consistency of Results, Directness of Evidence and Precision of Results. This quality control analysis highlighted moderate-to-high evidence quality for subcutaneous and ocular dirofilariasis treatment, with pulmonary cases showing moderate-quality evidence due to precision and follow-up gaps

RESULTS

Study Selection

Records identified: 320
Records after duplicates removed: 275
Full-text articles assessed for eligibility: 61
Studies included in review: 34, encompassing 145 cases of human dirofilariasis.

PRISMA Flow Diagram[35]



Data Analysis

1. Geographical Distribution

- **Europe:** prevalence of dirofilariasis cases are high across southern and eastern European countries, such as Italy, Greece, Spain, and France. These areas are often associated with warmer climates, which are conducive to the life cycle of the vector species (such as mosquitoes) that transmit Dirofilaria. Studies like those by Toma et al. (2011) and Serio et al. (2015) point towards the rising cases in Italy, where Dirofilaria repens is common.
- **Asia:** South Asian countries, particularly India and Sri Lanka, have been mentioned in multiple reports. Subcutaneous dirofilariasis is predominantly endemic in Kerala, India, with several cases documented in references like Jayakumar et al. (2011) and Srinivasan et al. (2018). The high humidity, tropical conditions, and mosquito vectors had been found to have a significant contribution to this prevalence.
- **North America:** Pulmonary dirofilariasis has been reported in the United States of America, particularly Florida and California, and due to Dirofilaria immitis, with emphasis in studies by Maguire (2000) and Kashyap et al. (2020). This is thought to be due to the sizable populations of domestic animals (especially dogs), which serve as hosts for the larvae.
- **Middle East:** Israel (Schwartz et al., 2020) has documented cases, with ocular dirofilariasis as new, emerging infections. The warm climate with increase in urbanization may enhance disease transmission.
- **Latin America:** Brazil and other Latin American countries have reported cases of human dirofilariasis, especially pulmonary and ocular forms. Studies such as Teixeira et al. (2017) highlight the increasing recognition of the disease in this region.

Regions with Emerging Trends

- **Asia:** In India, Sri Lanka, and other parts of South Asia, the disease is emerging more frequently due to the tropical climate, high population density, and increasing interactions between humans and mosquitoes.
- **Eastern Europe:** Countries such as Ukraine, Russia, and Romania have recently reported more cases, likely due to changes in climate and greater awareness of the disease.
- **Middle East:** In Israel and Turkey, human cases are increasing, likely due to the increasing incidence of ocular dirofilariasis in areas with high urbanization and travel activity.
- **South America:** While still underreported, cases of pulmonary dirofilariasis are rising in Brazil and Argentina, with the disease becoming a larger concern due to increased mosquito populations and animal reservoirs.

2. Risk Factors

Overlaying Climate Factors

- **Temperature and Humidity:** Dirofilaria species are sensitive to temperature, with warm, humid climates providing optimal conditions for propagation of the mosquito vectors. Tropical and subtropical regions such as India, Brazil and Southern Italy are more prone to these diseases due to their persistent high humidity and temperatures.
- **Seasonality:** In regions such as Kerala and Brazil with their distinct rainy and dry seasons, the prevalence of dirofilariasis might increase during or after the rainy season, when mosquito populations peak. For instance, Jayakumar et al. (2011) reported higher rates of infection in Kerala during monsoon periods.
- **Vector Distribution:** Spread of vector species like Aedes and Culex mosquitoes is directly tied to climatic conditions. Warm and humid climates promote the breeding of these mosquitoes, thereby putting the transmission of dirofilariasis at risk. Urban extension and stagnant water bodies allow mosquito populations to flourish.
- **Climate Change Impact:** Changing climate patterns may also expand the geographical reach of dirofilariasis. Warmer temperatures and shifting rainfall patterns could modify the distribution of mosquitoes and the parasitic larvae, thus allowing the emergence of new endemic areas.

Socio-Economic Factors

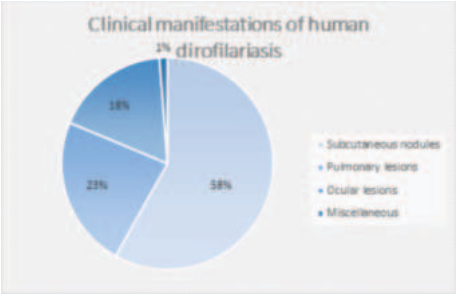
- **Urbanization and Migration:** Urbanisation and migration increase the risk of disease spread, including dirofilariasis. Mosquitos breed in densely populated urban areas with poor waste management. Migration from endemic to non-endemic places may also contribute to potentially disseminating Dirofilarial infection to new locations.
- **Animal Reservoirs:** Mosquitoes spread Dirofilaria immitis (heartworm) in places with a high pet population, particularly in dogs. In certain regions of North America and Europe, where human-wildlife interactions and pets residing at homes raise the risk of transmission, this situation is especially concerning.
- **Healthcare Access and Awareness:** In locations with limited healthcare access or lower awareness, such as rural India, Sri Lanka, and Africa, Dirofilaria infections may go untreated or misdiagnosed, leading to underreporting. In resource-limited environments, the lack of adequate diagnostic instruments may cause early detection to be delayed.
- **Economic Development and Prevention:** Developed healthcare infrastructures in Western Europe, Israel, and the United States have led to a higher number of reported cases, likely due to improved diagnostic techniques and increased awareness. Meanwhile, underreported cases in undeveloped nations occur due to inadequate surveillance systems.

Impact of Climate and Socio-Economic Factors

- **Growth of Vector Populations:** As a result of global warming, a variety of Dirofilaria species are welcomed in previously unaffected areas, and their representations there are altered. New geographical locations, such as Eastern Europe and the Middle East, are seeing an increase in pulmonary dirofilariasis isolates.
- **Human-Wildlife-Vector Interaction:** As more people move into formerly unoccupied areas or participate in outdoor activities like camping and trekking (Brazil, India), they become more exposed to mosquito vectors, increasing the risk of transmission.
- **Pet Ownership:** Increased pet ownership in North America and Europe, owing to increased human-animal interaction, exacerbates the chances of human infection, particularly Dirofilaria immitis. Socioeconomic growth allows for better control of a wide range of ailments, while also at the same time, increase in human-animal interaction produce new chances for disease transmission.

3. Clinical Manifestations

- **Subcutaneous:** Out of the 145 cases reviewed, 83 cases amounting to 57% presented as subcutaneous nodules, often on the face, arms, or chest with reports spanning across regions, particularly in Europe, India, and Brazil. Patients typically noticed a slow-growing, painless lump. However, due to wide differences concerning anatomical site and types of dirofilariasis, there is much variety to the accompanying symptoms.
- **Pulmonary:** A smaller subset of the cases -22% of cases [33 cases out of 145] presented with lung lesions, often found incidentally on chest imaging, typically reported in North America and Europe. Symptoms, when present, included cough and chest discomfort.
- **Ocular:** 14% of cases involved ocular infection, often presenting as orbital pain, redness, or visual disturbances. Less common but significant cases, especially in South Asia and parts of Europe.
- **Miscellaneous:** 1 % [4 out of 145] of reported cases showed miscellaneous presentations like meningoencephalitis (Poppert et al. (2009)) and breast lump misdiagnosed as possible malignancy.



4. Diagnosis

The reviewed studies utilized a combination of diagnostic methods to identify Dirofilaria infections. Clinical examination often relied on non-specific symptoms like subcutaneous nodules, ocular involvement, or pulmonary lesions, which can mimic other conditions and lead to misdiagnosis [tuberculosis, neoplasms etc].

Histopathological confirmation has been widely reported upon and considered the gold standard, involved the identification of the worm or its fragments in excised tissues, providing high specificity and the ability to differentiate between D. repens and D. immitis. However, this method requires invasive procedures and specialized histo-pathological expertise. [8,11]

Imaging techniques, such as chest X-rays, CT scans, and ultrasound, were used to detect pulmonary nodules or subcutaneous masses, but lacked specificity and required histopathological confirmation to differentiate from other lesions. [17,27]

Serological testing had limited use due to cross-reactivity issues with other helminths, and challenges with low sensitivity and specificity. [14] Molecular techniques, particularly Polymerase Chain Reaction (PCR), have gained increasing utilization to identify species-specific DNA, offering high sensitivity and specificity, and the advantage of being non-invasive. [12,26] However, these techniques require advanced laboratory setups, which may not be widely accessible in endemic regions. Finally, fine needle aspiration cytology (FNAC) has been effective in diagnosing subcutaneous cases, being less invasive than biopsy, but may be inconclusive in cases with minimal parasite material. [15,32]

Table 1: Showing Comparative Analysis Of Diagnostic Methods Used

Diagnostic Method	Accuracy	Reliability	Limitations	Reported Cases
Histo-pathology	High	High	Invasive, requires excision and expertise	Most widely used (Serio et al., Smitha et al.)
Imaging Techniques	Moderate	Moderate	Non-specific for Dirofilaria infections	Kashyap et al., Sundararajan et al.
PCR	Very High	High	High cost, limited availability	Srinivasan et al., Santos et al.
Serological Testing	Low	Low	Cross-reactivity with other helminths	Wang et al., Boeckh et al.
Cytology (FNAC)	Moderate	Moderate	Requires adequate parasite material	Singh et al., Ray et al.

5. Treatment and Outcomes

In practically all of the evaluated studies, surgical excision has been reported as the major therapeutic technique for subcutaneous dirofilariasis in order to remove localised nodules. [4, 18] With its high

success rates, this technique guarantees total elimination of the parasite and the tissue reaction zones around it. Ivermectin or albendazole are examples of supplementary antiparasitic medications that are preferably used to stop larval migration or guarantee total clearance. Recurrence is uncommon and usually associated with reinfection in endemic areas, and outcomes are good, with nearly 100% remission after surgery. [18] There are rarely any complications, only minor scarring or localised infections.

In pulmonary dirofilariasis, small, asymptomatic nodules usually resolve spontaneously without intervention, necessitating a more conservative approach of surveillance. [6] Surgical resection, like lobectomy or segmentectomy, is recommended for nodules that are symptomatic or when it is necessary to rule out malignancies. [16] Surgical treatment has a high resolution rate (90-95%), while spontaneous resolution was observed in 60-70% of observation cases. Recurrence is uncommon in surgically treated patients, however new nodules might develop in observation cases in endemic areas. Complications, such as pneumothorax, are rare, but might arise in intricate resections.

Surgical removal is the only way to eliminate the worms and restore eye function in cases of ocular dirofilariasis. Microsurgical procedures are used to minimize trauma. Adjunctive antiparasitic therapy is less usually utilised, although it should be evaluated in cases when there is inflammation or migration. When treated early, the success rate ranges from 98-100%, and no recurrences have been reported. Minor scarring or vision loss are possible concerns, although quick management has resulted in no serious ocular injury. [10,27]

In conclusion, treatment options for dirofilariasis are tailored to the unique clinical presentation, with surgical excision, observation, and microsurgical removal serving as the key modalities. The outcomes are generally positive, with high success rates and limited recurrence, while problems might occur in complex instances. Prompt diagnosis and effective management are critical to ensuring the best possible patient outcomes.

DISCUSSION

The spread of dirofilariasis is heavily influenced by geography and socioeconomic factors. Dirofilaria has expanded rapidly in regions with favorable climatic circumstances, such as tropical, subtropical, and temperate zones, owing to increased vector populations, migration, urbanization, and shifting human-wildlife interactions. The disease is more commonly recorded in Europe, Asia, and North America, although its prevalence is increasing in emerging countries such as the Middle East and South America. Researchers can forecast where future outbreaks will occur by overlaying climatic change and socioeconomic growth with regional disease trends, thereby informing public health policies for prevention and detection. This analysis emphasizes the significance of ongoing global surveillance, improved diagnostic techniques, and awareness initiatives to combat the zoonotic threat of dirofilariasis.

Temporal trends show an increase in case reports, particularly after 2010, as well as a greater understanding of peculiar presentations, such as ophthalmic, pulmonary, and invasive types. Traditional endemic regions, such as Italy, India, and the Americas, continue to remain significant contributors, while rising instances in Central Europe, Southeast Asia, and the Middle East indicate the establishment of new hotspots.

While histopathology continues to remain the gold standard for detecting human dirofilariasis, the increasing availability of molecular diagnostics such as PCR is revolutionizing the field with unprecedented precision. Combining imaging techniques with minimally invasive approaches like fine-needle aspiration cytology (FNAC) can aid in early detection, especially in endemic areas. Enhanced diagnostic capacity, coupled with global surveillance efforts, is essential to mitigate the burden of this emerging zoonotic disease.

Human dirofilariasis is effectively treated with surgical excision or careful observation based on clinical presentation. Pulmonary and subcutaneous cases demonstrate excellent outcomes with low recurrence rates, while ocular cases require urgent surgical attention. Adjunctive therapies, though not always necessary, can enhance outcomes in select cases. Future research should focus on long-term outcomes and optimizing therapies for atypical presentations.

For primary screening, healthcare providers should utilize imaging techniques (ultrasound/CT) combined with cytology (FNAC) to localize lesions and provide preliminary evidence. For confirmatory diagnosis, histopathological examination should be employed when feasible. In resource-limited settings, PCR should be prioritized as it offers high specificity with non-invasive sampling. Furthermore, PCR should be considered for species identification, particularly in rare or atypical cases, to guide management strategies.

Surgical excision remains the treatment of choice for subcutaneous cases, given its curative potential and minimal recurrence rates. Adjunctive antiparasitic therapy may be considered in endemic regions to prevent reinfection. For pulmonary cases, observation with periodic imaging is recommended for asymptomatic nodules, while surgical resection is indicated for symptomatic or diagnostic confirmation cases. Overtreatment should be avoided in spontaneously resolving lesions. In ocular cases, early surgical intervention is crucial to prevent vision loss and complications, and adjunctive anti-inflammatory therapy may be used in cases with severe inflammation.

CONCLUSION

Human dirofilariasis is an emerging zoonotic infection with distinct geographic patterns and clinical presentations. While infections are typically benign, they pose diagnostic challenges due to nonspecific symptoms and limited diagnostic tools. Surgical excision remains the cornerstone of treatment, with excellent prognosis post-removal. Future directions include the development of cost-effective, rapid diagnostic kits (e.g., species-specific serological or molecular assays), the implementation of training programs to improve the availability of histopathological expertise in endemic areas, and increased awareness, especially in endemic regions, with further studies on diagnostic methods and potential medical therapies. Prevention and recurrence mitigation strategies involve improved awareness and vector control in endemic regions, as well as routine follow-ups for early detection of reinfection or new lesions.

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