UNIVERSITI PUTRA MALAYSIA

RETROSPECTIVE STUDY ON FELINE SPOROTRICHOSIS DIAGNOSED AT THE UNIVERSITY VETERINARY HOSPITAL, UNIVERSITI PUTRA MALAYSIA FROM 2018 TO 2022

OOI HAN BING

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OOI HAN BING

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DEGREE OF DOCTOR OF VETERINARY MEDICINE

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CERTIFICATION

It is hereby certified that we have read this project paper entitled “Retrospective Study on Feline Sporotrichosis Diagnosed at the University Veterinary Hospital, Universiti Putra Malaysia from 2018 to 2022”, by Ooi Han Bing and in our opinion it is satisfactory in terms of scope, quality, and presentation as partial fulfillment of the requirement for the course VPD 4999 – Final Year Project.

DR. CHAN WEI YEE
DVM (UPM), MVM (UPM), PhD (Adelaide, Australia)
Senior Lecturer,
Companion Animal Medicine and Surgery,
Faculty of Veterinary Medicine,
Universiti Putra Malaysia
(Supervisor)

ASSOCIATE PROFESSOR DR. GAYATHRI THEVI SELVARAJAH
DVM (UPM),
PhD (Utrecht, Netherlands)
Senior Lecturer,
Department of Veterinary Clinical Studies
Faculty of Veterinary Medicine
Universiti Putra Malaysia
(Co-Supervisor)

DR. SHARINA OMAR
DVM (UPM),
PhD (Leicester, UK)
Senior Lecturer,
Department of Veterinary Pathology & Microbiology
Faculty of Veterinary Medicine
Universiti Putra Malaysia
(Co-Supervisor)

DR. AZALEA HANI OTHMAN
DVM (UPM),
MPhil (Queensland),
PhD (UPM)
Senior Lecturer,
Department of Veterinary Laboratory Diagnosis
Faculty of Veterinary Medicine
Universiti Putra Malaysia
(Co-Supervisor)

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ABSTRAK

Abstrak daripada kertas projek yang dikemukakan kepada Fakulti Perubatan Veterinar untuk memenuhi sebahagian daripada keperluan kursus VPD 4999 – Projek Ilmiah Tahun Akhir.

KAJIAN RETROSPEKTIF MENGENAI SPOROTRICHOSIS FELIN YANG DIDIAGNOSIS DI HOSPITAL VETERINAR UNIVERSITI, UNIVERSITI PUTRA MALAYSIA DARI TAHUN 2018 HINGGA 2022

Oleh

Ooi Han Bing

2023

Penyelia: Dr. Chan Wei Yee

Sporotrichosis ialah jangkitan kulat yang disebabkan oleh kulat dimorfik, kompleks *Sporothrix schenckii* yang biasa dilaporkan dalam kucing dan manusia terutamanya di kawasan tropika. Kajian ini berfungsi sebagai lanjutan penting, merapatkan jurang maklumat dalam penyelidikan sporotrichosis kucing melangkaui tahun 2017, berikutan kajian retrospektif terdahulu yang dilakukan di Hospital Veterinar Universiti (UVH), Universiti Putra Malaysia (UPM). Tujuan kajian adalah untuk menentukan prevalens, ciri klinikal, hasil rawatan dan faktor prognostik kucing yang didiagnosis dengan sporotrichosis di UVH, UPM dari Januari 2018 hingga Disember 2022. Rekod perubatan disemak secara retrospektif dan data yang dikumpul telah dijadualkan menggunakan Hamparan Microsoft Excel. Analisis statistik diskriptif selanjutnya

dikira menggunakan perisian IBM® SPSS® Versi 27. Kelaziman sporotrichosis kucing ialah 1% (244/24,317) dalam tempoh lima tahun ini. Selain itu, tahun 2020 menyaksikan penurunan (n=24) dalam kes sporotrichosis yang dilaporkan, yang boleh dikaitkan dengan pelaksanaan Perintah Kawalan Pergerakan (PKP) semasa pandemik COVID-19, yang mengehadkan pergerakan dan interaksi sosial. Antara kes sporotrichosis kucing di UVH, majoriti (56%) adalah kes pendapat kedua atau rujukan. Umur median kucing yang terjejas didapati 2 tahun, dengan jantan utuh merangkumi 39% daripada kes keseluruhan. Domestic Shorthair (DSH) adalah baka dominan (80%), dan 29% daripada kucing yang terjejas adalah perayau bebas, dengan 45% tinggal di rumah berbilang kucing. Lesi ulseratif (66%) adalah ciri klinikal yang paling lazim, dengan distribusi lesi biasanya di bahagian hidung (20%), telinga (12%), kaki belakang (10%), dan kaki depan (10%). Teknik diagnostik yang digemari oleh doktor dalam UVH adalah sitologi melalui kesan smear (72%) berbanding dengan kultur kulat (2%). Itraconazole adalah rawatan antikulat yang paling biasa (98.6%) diberikan. Bagi kucing yang berjaya pulih daripada sporotrichosis, masa median untuk penyembuhan klinikal ialah 68 hari. Di antara 244 kes sporotrichosis, hanya 25 kes menunjukkan remisi dengan majoriti (72%) mempunyai ≤ 3 lawatan semula ke UVH. Kesimpulannya, kajian ini memberikan pandangan berharga tentang sporotrichosis kucing, menjelaskan kelaziman, ciri klinikal dan pengurusannya dari 2018 hingga 2022, dengan pemerhatian ketara termasuk kadar kelaziman 1% dan kesan pandemik 2020 ke atas kes yang dilaporkan.

Kata kunci: *Sporothrix*, kucing, luka, Malaysia, itraconazole

ABSTRACT

An abstract of the project paper presented to the Faculty of Veterinary Medicine in partial fulfillment of the course VPD 4999 - Final Year Project.

RETROSPECTIVE STUDY ON FELINE SPOROTRICHOSIS DIAGNOSED AT THE UNIVERSITY VETERINARY HOSPITAL, UNIVERSITI PUTRA MALAYSIA FROM 2018 TO 2022

by

Ooi Han Bing

2023

Supervisor: Dr. Chan Wei Yee

Sporotrichosis is a fungal infection caused by the dimorphic fungi, *Sporothrix schenckii* complex commonly reported in cats and humans, especially in tropical regions. This study serves as a crucial extension, bridging the information gap in feline sporotrichosis research beyond the year 2017, following previous retrospective studies done at the University Veterinary Hospital (UVH), Universiti Putra Malaysia (UPM). This study aims to determine the prevalence, clinical characteristics, treatment outcomes and prognostic factors of cats diagnosed with sporotrichosis at the UVH, UPM from January 2018 to December 2022. Medical records were retrospectively reviewed and data collected was tabulated using Microsoft Excel

Spreadsheet Software and further statistical analyses were calculated using IBM® SPSS® software Version 27. The prevalence of feline sporotrichosis was 1% (244/24,317) during these five years. It was worth noting that the year 2020 witnessed a decline (n=24) in reported sporotrichosis cases, which could be attributed to the implementation of Movement Control Orders (MCO) during the COVID-19 pandemic, limiting mobility and interactions. Among the feline sporotrichosis cases at the UVH, the majority (56%) were second opinion or referral cases. The median age of affected cats was found to be 2 years, with intact males comprising 39% of the cases. The Domestic Shorthair (DSH) breed was predominant (80%), and 29% of the affected cats were free roamers, with 45% residing in multi-cat households. Ulcerative lesions (66%) were the most prevalent clinical characteristic, with common distribution sites including the nose (20%), ear (12%), hindlimb (10%), and forelimb (10%). The diagnostic technique favoured by clinicians in UVH was cytology by impression smear (72%) as compared to fungal culture (2%). Itraconazole was the most common (98.6%) antifungal treatment administered. For cats that successfully recovered from sporotrichosis, the median time to clinical cure was 68 days. Among 244 cases of sporotrichosis, only 25 cases showed remission with the majority (72%) having ≤ 3 revisits to UVH. In conclusion, this study provides valuable insights into feline sporotrichosis, shedding light on its prevalence, clinical features, and management from 2018 to 2022, with notable observations including a 1% prevalence rate and the impact of the 2020 pandemic on reported cases.

Keywords: *Sporothrix*, cat, wound, Malaysia, itraconazole

1.0 INTRODUCTION

Sporotrichosis is a fungal infection that can affect both animals and humans. It has been reported in humans and several animal species, including cats, dogs, armadillos, horses, mules, donkeys, chimpanzees, cattle, goats, pigs, mice, rats, hamsters, dolphins, foxes, camels, and fowl (Schubach *et al*., 2012). Sporotrichosis in animals was distributed worldwide based on the study by Morgado *et al.* (2022), mainly in South America followed by Asia and Europe. This infection is caused by multiple species of *Sporothrix* which are distributed worldwide according to De Beer *et al.* (2016). Naturally, *Sporothrix* can be found in the soil and on the surface of plants (Barros *et al.*,2011).

Globally, *Sporothrix* consists of multiple species which are pathogenic namely *S. brasiliensis*, *S. schenckii*, *S. globosa*, and *S. luriei* (Morgado *et al.*,2022). In Malaysia, the most ubiquitous strain causing feline sporotrichosis with low susceptibility to major antifungal classes is *Sporothrix schenckii sensu stricto* (Han & Kano, 2020). It is important to note that *Sporothrix schenckii sensu stricto* was reported in Asia according to Zhou *et al.* (2013). However, this common type of *Sporothrix schenckii sensu stricto* clinical clade C, found in Asia, is different from the clinical clade D specifically encountered in Malaysia (Zhou *et al.*, 2013). This demonstrates that the species is continuously changing, adapting through a process of purifying selection, and expanding its population based on local environmental or host selection pressures (Han & Kano, 2020).

The zoonotic potential of sporotrichosis raises a prominent public health concern as it can be transmitted to humans via multiple modes. This is especially common in owners with a cat that has an active infection of sporotrichosis. A study by Morgado *et al.* (2022) has shown that the rise in the number of cats infected with sporotrichosis

correlates with the increase of this infection in humans. Zoonotic infection can occur from cats to humans and has been reported without evidence of trauma despite the risk of transmission being higher in the presence of bites, scratches, or contact with the fungus in the environment (Gull, 2023). This poses the importance of proper handling of sporotrichosis infected cat by isolating the cat, handling the cat with gloves and disinfecting the surface that has come in contact with the cat (Lloret *et al.*, 2013).

The cases of sporotrichosis are usually found in cats due to their behaviours and environmental exposure. The primary mode of transmission is traumatic inoculation of fungal conidia from bites, scratches, and contact with infected animals (Lloret *et al.*, 2013). The transmission of sporotrichosis to other animals is enhanced by the great amount of fungus present in the cat's lesions (Marques *et al.*, 1993). Therefore, the behaviours of the cat, such as licking, biting, and scratching, can increase the chances of the fungus entering the cat's body through open sores or wounds (McVey *et al.*, 2013). Furthermore, the environmental exposure of cats to the fungus, such as contact with contaminated soil and plant material, can also lead to infection of feline sporotrichosis (Rodrigues *et al.*, 2016).

There are three clinical manifestations of feline sporotrichosis which are the fixed cutaneous form, the lymphocutaneous form, where the agent expands through lymphatic vessels and the disseminated form, involving infection of multiple organ systems (Pacheco *et al.*, 2003). Localized cutaneous lesions include multiple ulcerated nodules with hemorrhagic drainage, usually on the head, distal limbs, and tail, that spread to other body parts (Han & Kano, 2020).

The diagnosis of feline sporotrichosis relies on laboratory testing because the clinical signs cannot rule out other differential diagnoses. The differential diagnosis of cutaneous lesions similar to feline sporotrichosis includes bacterial pyoderma,

mycobacteriosis, actinomycosis, cryptococcosis, foreign body and squamous cell carcinoma (Peaston, 1993). *Sporothrix* spp. organisms present in high numbers in infected feline patients thus making them easily detectable via cytology (Han & Kano, 2020). Therefore, routine in-clinic cytology with Romanowsky-type stain is the preferred diagnostic option for private veterinarians in Malaysia for a rapid diagnosis (Han & Kano, 2020). Under microscopic observation, *Sporothrix* yeast will be found located intra and extracellularly, in pleomorphic shapes ranging from cigar-shaped to round or oval, with a clear halo around a pale blue cytoplasm (Han & Kano, 2020).

Antifungal drugs used in clinical practice to treat feline sporotrichosis are azoles, such as itraconazole, ketoconazole, fluconazole, potassium iodide, and amphotericin B. Itraconazole is considered the first-line antifungal drug. Unfortunately, the success rate of therapy is relatively low and requires regular long-term treatment because of the low susceptibility of *Sporothrix* spp. to drugs (Madrid *et al.*, 2010; Siew, 2017; Nakasu *et al.*, 2020).

Feline sporotrichosis raises a significant public health concern due to its potential for zoonotic transmission. Consequently, it is necessary to understand the prevalence, clinical characteristics, treatment outcomes, and prognostic factors of feline sporotrichosis to improve the management and control of this disease in both animals and humans. This study can provide recent information on the prevalence and clinical characteristics of feline sporotrichosis in this region and identify any changes in the pattern of the disease that could indicate new emerging strains or trends. Additionally, this study may provide insights into the effectiveness of current treatment options and indicate areas for improvement in the management of the disease. Thus, this retrospective study on feline sporotrichosis is justified as it can contribute to the

knowledge of the disease and improve the management and control of feline sporotrichosis in this region.

The objective of this study is to determine the prevalence, clinical characteristics, treatment outcomes and prognostic factors of cats diagnosed with sporotrichosis at the University Veterinary Hospital (UVH), Universiti Putra Malaysia (UPM) from 2018 to 2022.

The hypotheses for this study are:

1. There was an increase in the number of cases of feline sporotrichosis at the University Veterinary Hospital, Universiti Putra Malaysia from 2018 to 2022.
2. Ulcerated wound was the most common type of lesion for feline sporotrichosis.

2.0 LITERATURE REVIEW ON FELINE SPOROTRICHOSIS

2.1 Epidemiology and demographic

Feline sporotrichosis is primarily found in tropical to sub-tropical regions (Han & Kano, 2020). According to a systematic review conducted by Morgado *et al.* (2022), the majority of sporotrichosis cases in animals from the years 2007 to 2021 were concentrated in South America, with a significant number of cases also reported in Asia. This trend underlines the climatic conditions favourable to fungal growth and transmission in the regions. Notably, the most identified species causing sporotrichosis were *Sporothrix brasiliensis*, isolated from cats in Brazil and *Sporothrix schenckii* isolated from cats in Malaysia (Morgado *et al.*, 2022).

2.2 Form and symptoms

Sporotrichosis can be categorized into three forms: cutaneous, lymphocutaneous, and disseminated. In the cutaneous form, typical regions for bites and scratches during fights such as the head, limbs, and tail-base region all have numerous, ulcerated, and crusted nodules, draining tracts, and abscesses or cellulitis. (Lloret *et al.*, 2013). Lymphatic involvement may not be clinically apparent but can be detected histologically via biopsy or necropsy samples (Welsh, 2003; Crothers *et al.*, 2009). The disseminated form usually involves multiple organs, with the lungs and liver being the primary site of infection (Schubach *et al.*, 2004; Crothers *et al.*, 2009). Hematogenous dissemination can lead to widespread cutaneous lesions following the primary infection of the respiratory system, whereby the fungus can be cultured from blood (Schubach *et al.*, 2003; Lloret *et al.*, 2013).

2.3 Modes of transmission

The mycelial form of the organism enters the tissue through traumatic inoculation, transforms into the yeast form, and then multiplies locally to produce cutaneous nodules that are ulcerated, and exudative, involving the dermal and subcutaneous tissues. Discharging lesions, especially in cats, might be contagious due to the high microbe content of their exudates. The microorganism can be isolated from the nails of diseased cats and even healthy cats in touch with infected cats, implying the possibility of transmission. Internal infections, though uncommon, can occur through inhalation or ingestion (McVey *et al.,* 2013).

2.4 Current and advance diagnostic methods

According to Han and Kano (2020), private veterinarians in Malaysia favour standard in-clinic cytology with Romanowsky-type stain as a rapid diagnostic method. This is because *Sporothrix* spp. organisms are abundant and easily detected in cytological preparations, particularly from feline patients. Under microscopic observation, a cytology sample of *Sporothrix* spp. organisms with Romanowsky stain shows the organism as cigar-shaped, refractile and non-staining. Besides, a serological method is applicable in detection of the mycotic infection. A study by Alvarado *et al.* (2015) of an ELISA for the identification of *Sporothrix schenckii* antibodies showed good sensitivity and specificity (over 90%), suggesting that it could be used as a screening tool for feline sporotrichosis. Furthermore, a fungal culture is required as a confirmatory test for feline sporotrichosis, involving the demonstration of both mycelial and yeast phases of *Sporothrix* spp. to establish a definitive diagnosis (McVey *et al.,* 2013).

2.5 Therapeutics and clinical management

Feline sporotrichosis treatments include potassium iodide, azoles (ketoconazole and itraconazole), amphotericin B, terbinafine, local heat therapy, cryosurgery and surgical resection (Han & Kano, 2020). In cats, a 5-10 mg/kg oral dose of itraconazole produced a maximum plasma concentration of 0.7 ± 0.14 mg/L and was efficacious in treating sporotrichosis (Liang *et al.*, 2016). In cases where cats with sporotrichosis demonstrate inadequate response to itraconazole monotherapy, or naïve cats, especially ones with multiple cutaneous lesions, nasal mucosal lesions and/or respiratory signs, the combination of itraconazole (50–100 mg/day) and potassium iodide (2.5–20 mg/kg/day) was proven to increase the likelihood of recovery (Reis *et al.*, 2016; De Miranda *et al.*, 2018; da Rocha *et al.*, 2018).

2.6 Prognosis and clinical outcome

A good prognosis is generally expected when treatment duration is appropriate, and owners follow the suggested regimen. However, the prognosis turns adverse in cases of disseminated infections or if treatment is abruptly stopped before the indicated course of treatment is completed (Welsh, 2003; Crothers *et al.*, 2009). On the other hand, the prognosis of feline sporotrichosis in Malaysia appears poor to guarded due to the persisting challenge of cost, prolonged treatment time, danger of zoonotic transmission, and possible adverse effects to antifungals when given long-term (Han & Kano, 2020).

3.0 METHODOLOGY

3.1 Data collection

The data collection process started with thoroughly reviewing the master logbook for 5 years, from January 2018 to December 2022, at University Veterinary Hospital (UVH), Universiti Putra Malaysia (UPM), targeting cases identified through keywords such as “sporotrichosis,” “non-healing wound,” or “ulcerative wound.” Subsequently, case numbers associated with these instances were documented for subsequent retrieval of case files. A total of 382 case files were retrieved and subjected to a comprehensive review. From this pool, 244 case files confirmed with a diagnosis of sporotrichosis were included in this study.

Historical data include the date of diagnosis, signalment (breed, age, gender, neuter status, and demography), environment exposure (outdoor, indoor, and semi-roamer), management (multiple cat household or single cat household), source of infection (cat fights, contact with sick cats, presence of other clinical signs (respiratory signs or lymph nodes involvement), disease duration and treatment prior to presentation at UVH.

Clinical data consisted of physical examination findings such as type of lesions, distribution of lesions, and extracutaneous signs. Besides, the diagnostic methods utilised for these cases were also recorded such as cytology via impression smear, complete blood count and serum biochemistry. The treatment plan of the cases including the drugs (antifungal, anti-inflammatory, analgesic, or supplement) and procedures done were also taken into account.

3.2 Data tabulation and descriptive analysis

The collected data were organized and tabulated using Microsoft Excel spreadsheet software. Descriptive analyses, including frequencies, medians, and modes where applicable, were conducted using both Microsoft Excel and IBM® SPSS® Statistics program, version 27.

4.0 RESULTS

4.1 Prevalence

There were a total number of 24 317 cats presented to UVH, UPM in five years from January 2018 to December 2022. Out of the total, 244 cats were diagnosed with feline sporotrichosis. Thus, the prevalence of feline sporotrichosis diagnosed in UVH, UPM from January 2018 to December 2022 was calculated to be 1%.

4.2 Frequency and Demography

From January 2018 to December 2022, 244 cases of feline sporotrichosis were diagnosed in UVH, UPM. Overall, the trend of the number of feline sporotrichosis cases diagnosed at UVH has declined over five years **(see Figure 1)**. The highest number of cases was in 2018 (n=81), while the lowest number of cases was in 2020 (n=28).

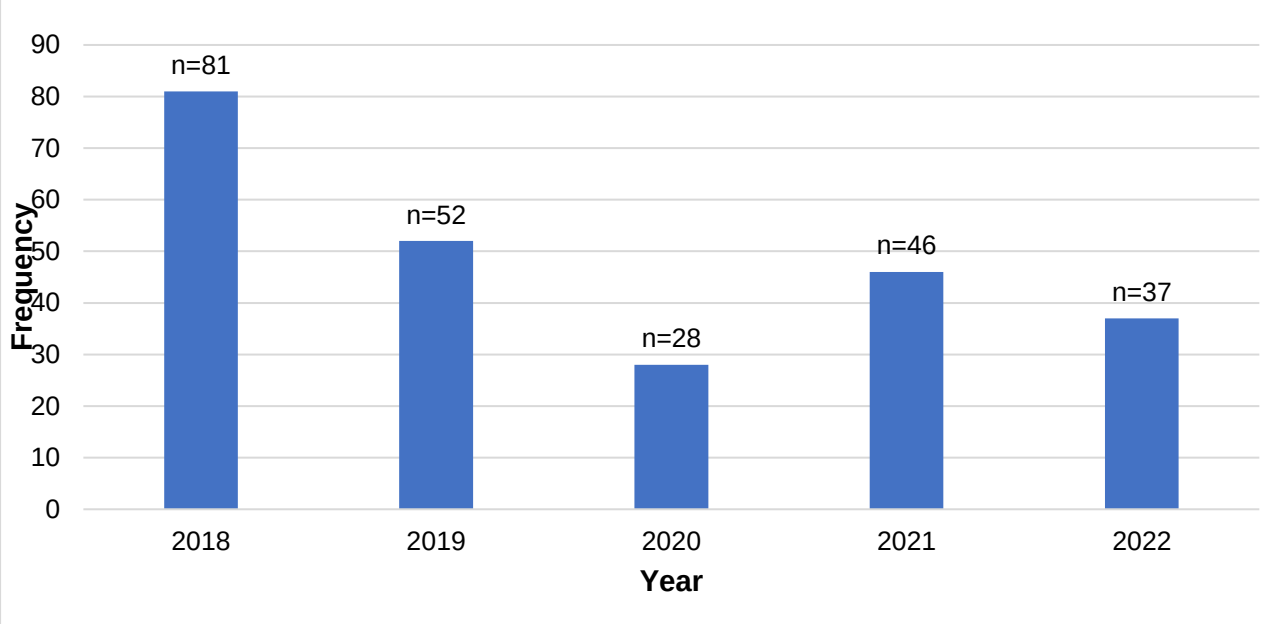

Figure 1: Number of new cases of feline sporotrichosis diagnosed at UVH from 2018 to 2022

The cats were then categorized according to the address of the owners. The cat came from 244 different addresses, consisting of 184 (75.4%) from the state of Selangor, 31 (12.7%) from Kuala Lumpur, 13 (5.3%) from Negeri Sembilan, 9 (3.7%) from Putrajaya and the remaining 7 (2.9%) from various places namely Pahang, Kelantan, Perak, Kedah or not stated. Out of these locations, Kajang was found to be having the highest percentage of representation among cats presented with feline sporotrichosis in UVH, accounting for 28 (11.5%) **(Table 1)**.

Table 1: Demography of cats from 244 residences

State	Location	Number (n)	Percentage (%)
Selangor	Ampang	4	1.64
	Bandar Puncak Alam	1	0.41
	Bangi	6	2.46
	Banting	3	1.23
	Batu Caves	4	1.64
	Bandar Baru Bangi	15	6.15
	Beranang	3	1.23
	Bestari Jaya	1	0.41
	Bukit Antarabangsa	1	0.41
	Cheras	6	2.46
	Cyberjaya	3	1.23
	Dengkil	4	1.64
	Gombok	1	0.41
	Hulu Langat	3	1.23
	Jenjarom	3	1.23
	Kajang	28	11.48
	Klang	4	1.64
	Kota Damansara	1	0.41
	Kuala Langat	1	0.41
	Kuang	2	0.82
	Medan Damansara	1	0.41
	Petaling Jaya	8	3.28
	Puchong	17	6.97
	Pulau Ketam	1	0.41
	Pusat Bandar Putra Permai	1	0.41
	Putra Perdana	1	0.41
	Putrajaya	1	0.41

	Salak Tinggi	1	0.41
	Semenyih	4	1.64
	Sepang	6	2.46
	Serdang	5	2.05
	Seri Kembangan	10	4.10
	Shah Alam	16	6.56
	Subang Jaya	2	0.82
	Sungai Besi	1	0.41
	Sungai Buloh	5	2.05
	Sungai Rambai	5	2.05
	Telok Panglima Garang	1	0.41
	Ulu Klang	3	1.23
	UPM	1	0.41
Total		184	75.4
Kuala Lumpur	Ampang	1	0.41
	Ampang Jaya	4	1.64
	Batu Caves	4	1.64
	Bukit Jalil	1	0.41
	Cheras	2	0.82
	Cheras Indah	1	0.41
	Damansara Heights	1	0.41
	Desa Tasik	1	0.41
	Kampung Pandan	1	0.41
	Kuchai Lama	1	0.41
	Petaling Jaya	2	0.82
	Pudu	1	0.41
	Setapak	3	1.23
	Setapak Garden	1	0.41
	Sri Petaling	1	0.41
	Sungai Besi	1	0.41
	Taman Desa Keramat	1	0.41
	Taman Keramat	1	0.41
	Taman Setiawangsa	2	0.82
	Wangsa Maju	1	0.41
Total		31	12.7
Negeri Sembilan	Bandar Enstek	1	0.41
	Lenggeng	1	0.41
	Mantin	2	0.82
	Nilai	3	1.23
	Seremban	5	2.05
	Sungai Gadut	1	0.41
Total		13	5.3

Putrajaya	Dengkil	1	0.41
	Presint 11	2	0.82
	Presint 15	1	0.41
	Presint 16	1	0.41
	Presint 17	1	0.41
	Presint 6	1	0.41
	Presint 8	2	0.82
Total		9	3.7
Pahang	Benta	1	0.41
	Raub	1	0.41
Total		2	0.82
Kelantan	Kota Bahru	1	0.41
Perak	Teluk Intan	1	0.41
Kedah	Sungai Petani	1	0.41
Not stated		2	0.82

Among the 244 cases, the majority (56%) were second opinion or referral cases, totalling 137 **(Figure 2)**. This aligns with the number of visits, as most cases (51%) sought consultation or diagnostic services at UVH only once **(Figure 3)**. Subsequently, many would likely return to the previous private clinic from which they were referred.

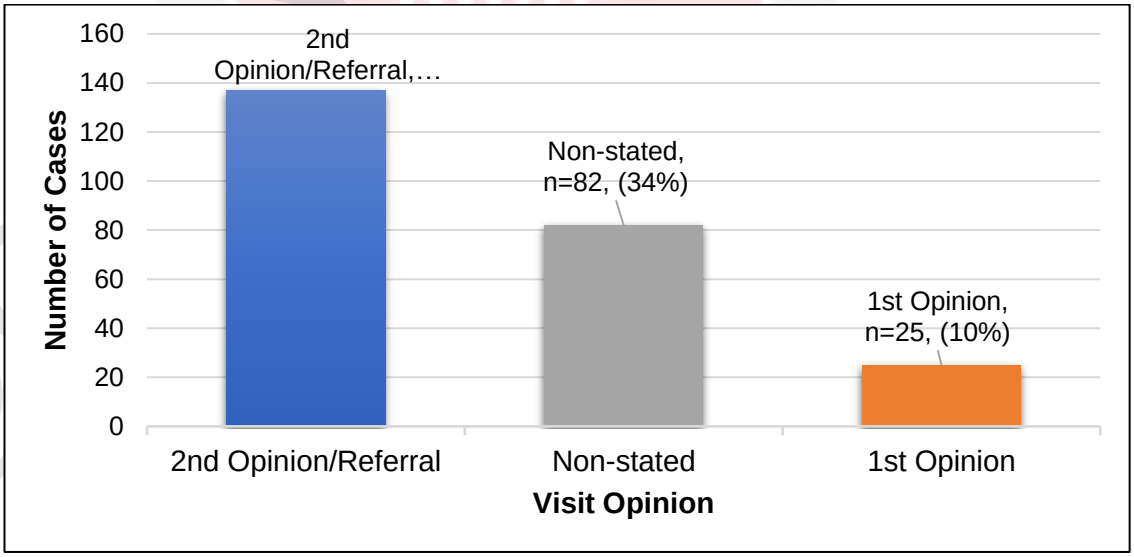

Figure 2: Number of visit opinions of feline sporotrichosis cases diagnosed at UVH from 2018 to 2022

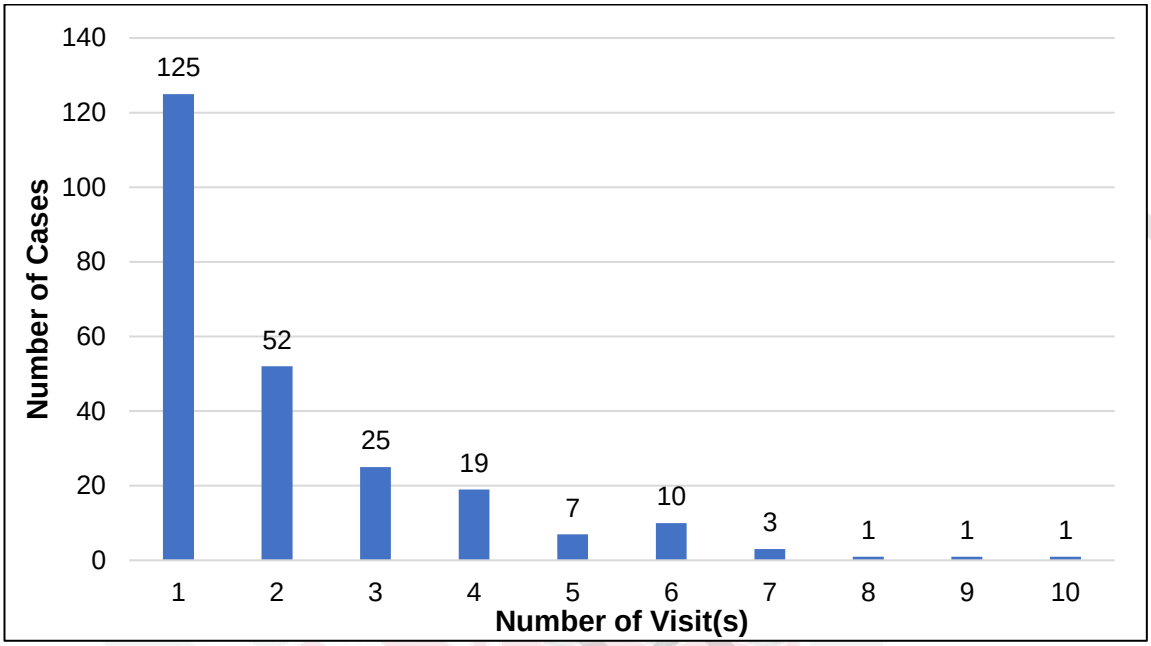

Figure 3: Number of visits of feline sporotrichosis cases diagnosed at UVH from 2018 to 2022

4.3 Signalment and Historical Data

The mode of the age of 244 cats diagnosed with sporotrichosis was 1 year old while the median age was 2 years old **(Figure 4)**. Male cats were over-presented (n=149, 61%) with 159 (65%) being sexually intact. Most of the cats were Domestic Shorthair (n=195, 80%) and outdoor cats (n=71, 29%). The management of the cat was mostly not recorded during consultation attributed to 114 (47%) of the cats **(see Table 2)**.

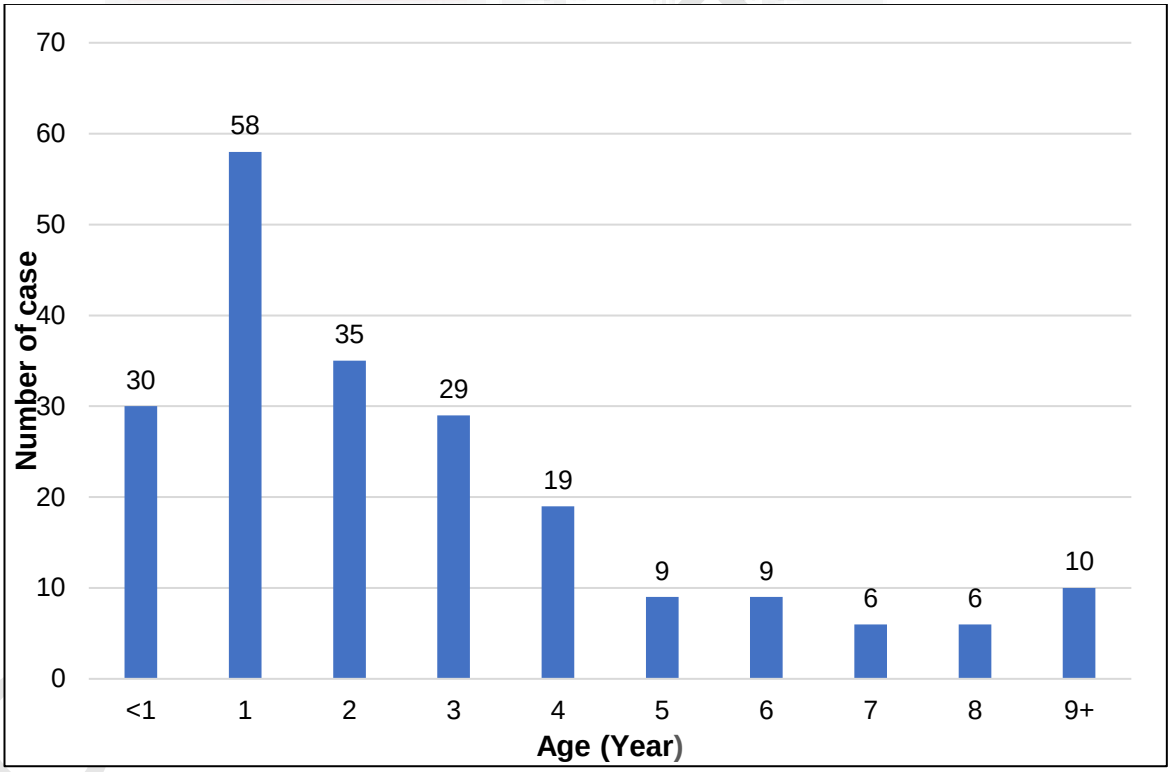

Figure 4: Distribution of feline sporotrichosis cases by age

Table 2: Signalment, management and environmental exposure for 244 cats diagnosed with sporotrichosis

Characteristics		**n**	**%**
Sex	Male	149	61
	Female	88	36
	Unidentified	7	3
Neutering status	Intact	159	65
	Neutered	85	35
Breed classifications	Domestic short hair	195	80
	Others	49	20
Environmental exposure	Outdoor	71	29
	Indoor	67	28
	Semi-roamer	61	25
	Not stated	48	18
Management	Multiple cat household	110	45
	Singe cat household	20	8
	Not stated	114	47

4.4 Clinical data

4.4.1 Lesion types and distribution

Ulcerative lesions (n=203, 66.34%) were the predominant cutaneous lesions, followed by mass (n=36, 11.76%), nodular (n=31, 10.13%), nasal swelling (n=17, 5.56%) and granulomatous inflammation (n=6, 1.96%) **(Table 4)**. Cutaneous lesion mainly distributed at the nose (n=123, 20.2%), followed by ear (n=71, 11.7%), hind limbs (n=62, 10.2%), and fore limbs (n=60, 9.9%) **(Figure 5) (Table 3).**

Figure 5: Number and percentage of cutaneous lesions distribution

Table 3: Number and percentage of cutaneous lesions distribution

Lesion Distribution	n	%
Nose/nostril	123	20.23
Ear	71	11.68
Hind Limb	62	10.20
Fore Limb	60	9.87
Distal extremities	38	6.25
Face	31	5.10
Eye/Periorbital	28	4.61
Flank/Abdomen	28	4.61
Tail	28	4.61
Head	25	4.11
Dorsum/Trunk	17	2.80
Mouth	16	2.63
Rump	14	2.30
Genitals	12	1.97
Axilla	10	1.64
Inguinal	10	1.64
Neck	10	1.64
Shoulder	10	1.64
Chest	7	1.15
Hip	4	0.66
Perineum	3	0.49
Ventrum	1	0.16

Table 4: Types of cutaneous lesions

Lesion Type	n	%
Ulcerative lesion	203	66.34
Mass	36	11.76
Nodular	31	10.13
Nasal swelling	17	5.56
Granulomatous inflammation	6	1.96
Wound with exposed bone	4	1.31
Maggot wound	3	0.98
Abscess	2	0.65
Crust	1	0.33
Cyst	1	0.33
Pedunculated mass	1	0.33
Nasal Polyp	1	0.33

4.4.2 Other clinical signs

Other clinical signs include respiratory signs and lymphadenopathy. Types of respiratory signs recorded mainly were sneezing (n=23), nasal discharge (n=13) and harsh lung sound (n=8) **(Figure 6)**. Submandibular lymph nodes (n=32) were also found to be mostly involved in the lymphadenopathy concurrent with sporotrichosis **(Figure 7)**.

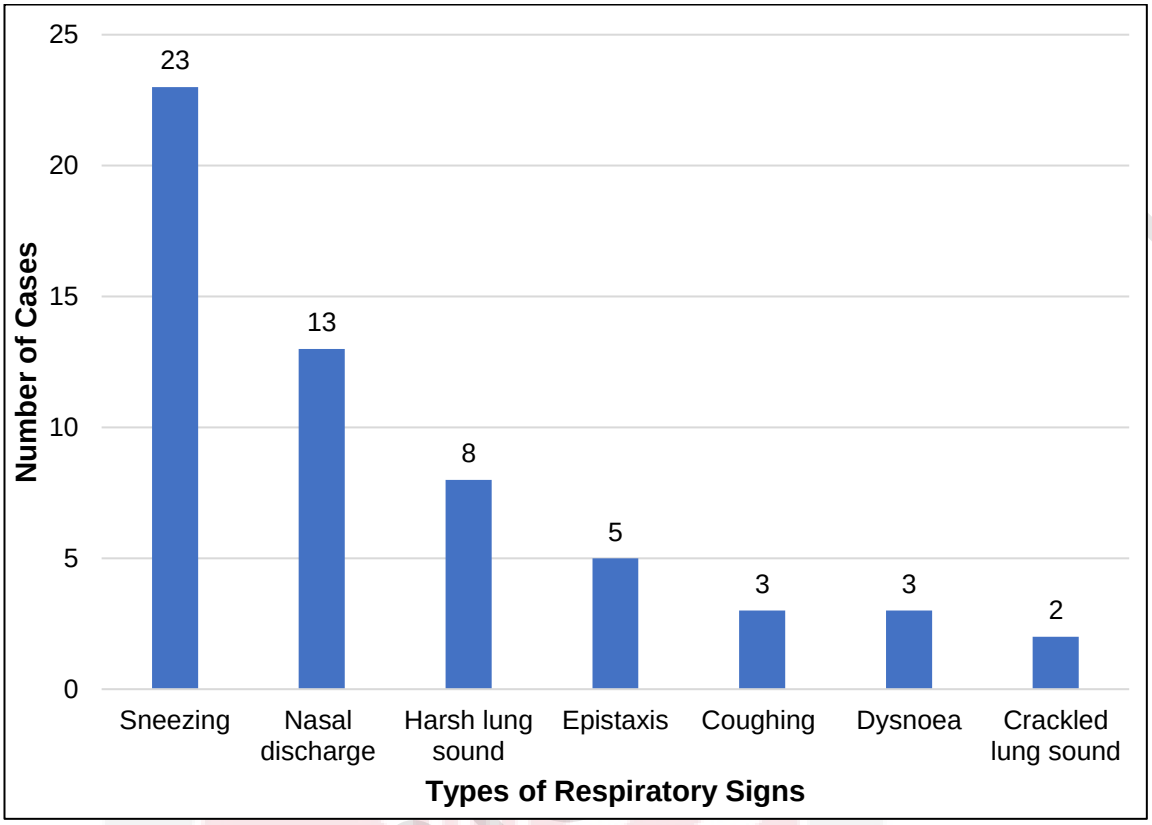

Figure 6: Number of cases with respiratory signs

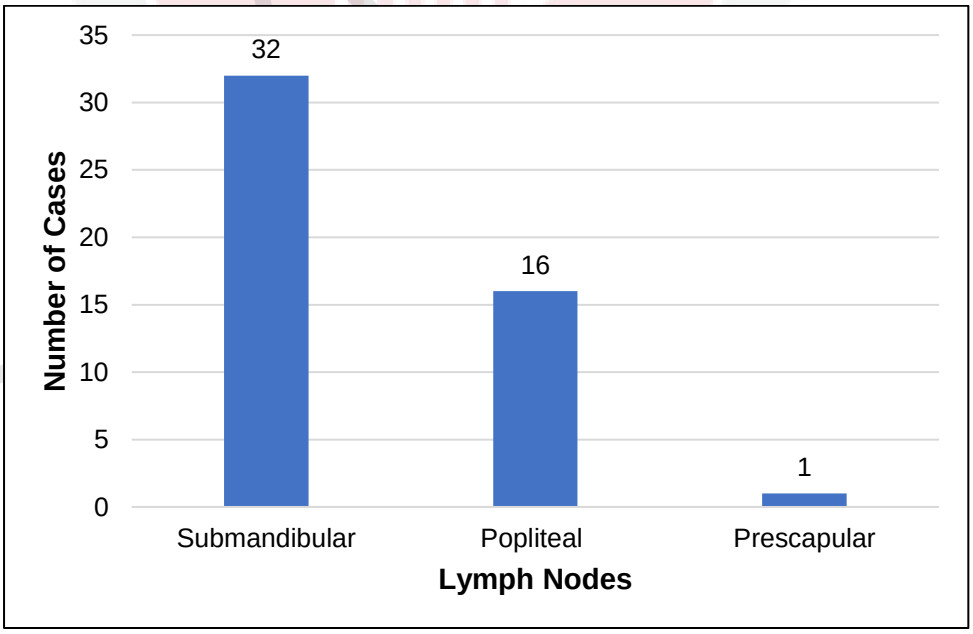

Figure 7: Involvement of lymph nodes

4.5 Diagnostic methods

4.5.1 Cytology and mycology

Cytology via impression smear was the most used diagnostic method for feline sporotrichosis cases in UVH **(Table 5)**. A clean glass slide is gently but firmly pressed on the ulcerative lesion **(Figure 8)** and stained by Diff-Quik, a modified Romanowsky stain. The slide can then be examined under a microscope for the presence of numerous cigar-shaped, oval or round budding yeast-like organisms with a single round pink nucleus surrounded by blue cytoplasm.

Figure 8: Cytology obtained by impression smear of the lesion

Table 5: Diagnostic techniques used in cats diagnosed with feline sporotrichosis

Diagnostic Technique	Number
Impression smear	217
Complete blood count	23
Serum biochemistry	21
Chest radiography	9
Fungal culture	7
Bacteria culture	6
Wood's lamp	4
Antibiotic susceptibility test	3
Fine needle aspiration	2
Urinalysis	2
Hair pluck	1

4.6 Therapeutic approaches

4.6.1 Antifungal therapies

Out of 244 cases of feline sporotrichosis presented to UVH, 217 cases (98.6%) were prescribed with itraconazole **(Figure 9)**. However, there were 27 cases whereby the oral antifungal therapies were not recorded because those cases came in only for consultation and some planned to board in different clinics. Of the 217 cases prescribed with itraconazole, Inox® was the generic drug used in 148 cases while the Sporanox® was the brand-name drug used in 48 cases. Notably, Inox® was switched to Sporanox® in 21 cases. Treatment with itraconazole was usually given at 10mg/kg bodyweight, once daily for 30 days whereby the client would need to bring the cat

back for a follow-up. Besides, itraconazole (Sporanox®) was then switched to ketoconazole (15mg/kg bodyweight twice daily) in two of the cases.

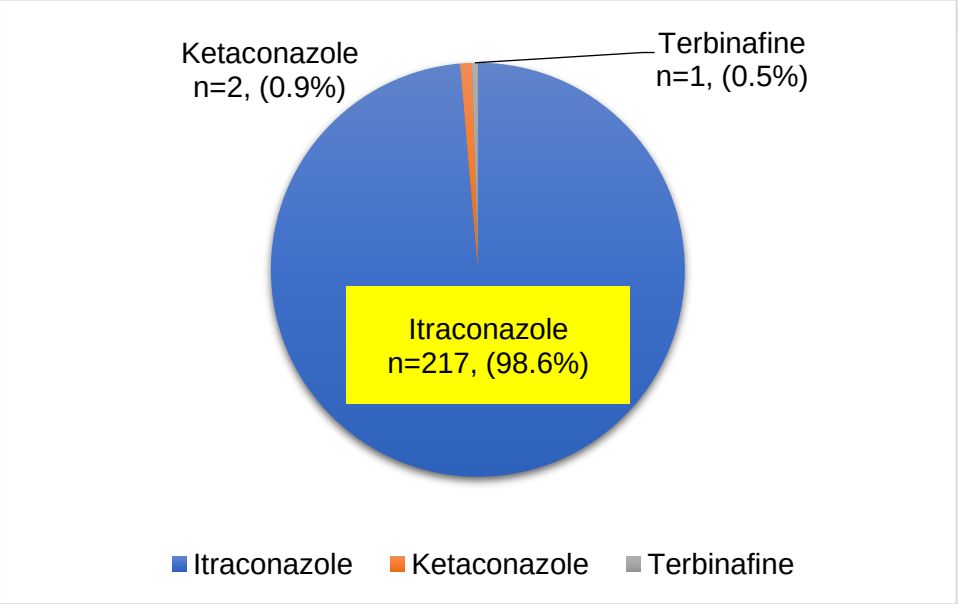

Figure 9: Oral antifungal therapies

4.6.2 Other therapies

Concurrent antibiotics were the most common treatment alongside antifungal therapies. The common systemic antibiotics used were amoxicillin/clavulanic acid (n=34), cephalexin (n=11) and amoxicillin (n=8). Subsequently, anti-inflammatory used was mostly serratiopeptidase (n=54). Following that, there were supplements prescribed which mainly targeted the liver (n=17) such as Samilyn® (n=4) and Glutamax forte (n=3); and the skin (n=4) namely Nutricoat® (n=3) and Coatex® (n=1). Detail breakdown of other therapies is demonstrated in **Table 6**.

Table 6: Other therapies used concurrently with antifungal treatment

Category	Group	Name	Number
Systemic antibiotic	Penicillin and Beta-lactamase inhibitors	Amoxicillin/ Clavulanic acid	34
	Cephalosporin	Cephalexin	11
	Penicillin	Amoxicillin	8
	Fluoroquinolone	Marbofloxacin	7
	Nitroimidazole	Metronidazole	7
	Tetracycline	Doxycycline	5
	Cephalosporin	Cefixime	2
	Fluoroquinolones	Enrofloxacin (Batyril®)	1
	Cephalosporin	Cefuroxime (Convenia®)	1
Total			76
Anti-inflammatory	Proteolytic enzyme	Serratiopeptidase	54
	Corticosteroid	Prednisolone	1
	Selective COX-2 inhibitor	Etoricoxib (Arcoxia®)	1
	Fenamate (NSAIDs)	Tolfenamic acid (Tolfedine®)	1
Total			57
Supplement	Multivitamins	Multivitamins	9
	Other vitamins	Vitamin B	8
	Other vitamins	Vitamin C	2

	Immune Booster	Vetri DMG®	5
	Liver	Samilyn®	5
	Liver	Glutamax™ forte	5
	Liver	Besame	2
	Liver	Liver supplement (not specified)	1
	Skin	Nutricoat®	3
	Skin	Coatex®	1
	Iron Supplement	Ferroctyes	1
Total			42
Topical antimicrobial	Antiseptic	Providone iodine	15
	Antifungal	Miconazole (Becarin®) cream	6
	Antibiotic	Gentamycin cream	4
	Antiseptic	Chlorhexidine (Hibiscrub®)	4
	Antiseptic	Hypermix®	2
	Antiseptic	Intrasite gel	2
	Antifungal/Antibacterial	Malaseb® shampoo	2
	Antibiotic/Corticosteroids	Betamethasone/ Gentamycin (Beagenta®) cream	1
	Antiseptic	Woundsarex™	1
Total			37
Antiparasitic	Endectocide	Advocate® Spot On	10
	Endoparasite	Drontal™	13

	Ectoparasite	Frontline® Spot On	7
	Endectocide	Ivermectin	4
	Endoparasite	Spot-On (Not specified)	1
Total			35
Antihistamine		Chlorpheniramine	31
		Cetirizine (Cetrizine®)	1
Total			32
Mucolytic		Bromhexine	18
Analgesic	Opiate	Tramadol	6

4.7 Clinical outcomes

Out of 244 cases, only 31 cases were reported with proper clinical outcomes recorded in the case files and the remaining 213 cases were lost to follow-up (**Figure 10**). A total of 25 cases were reported to recover from feline sporotrichosis with a median recovery time of 68 days. Unfortunately, six cases of feline sporotrichosis had gone through euthanasia.

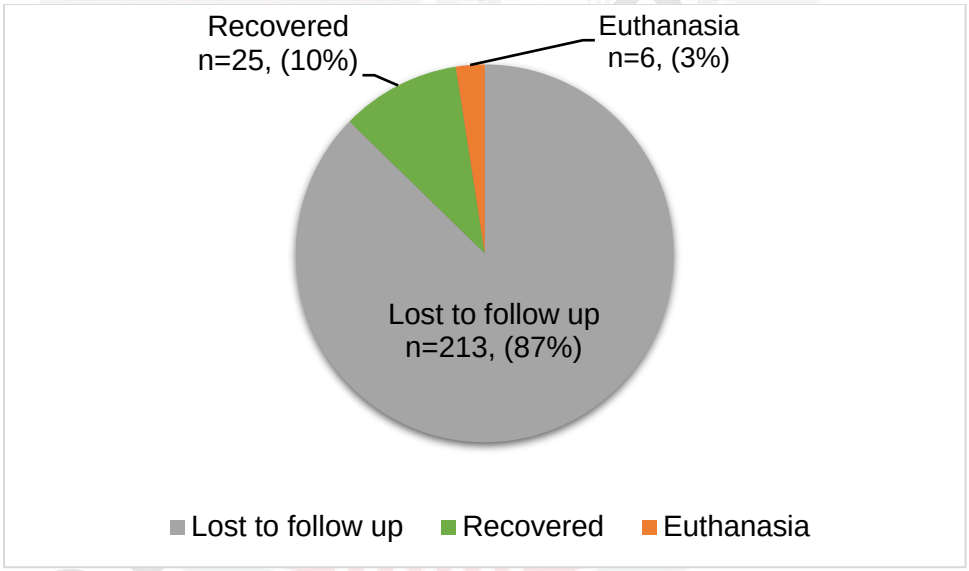

Figure 10: Clinical outcomes

5.0 DISCUSSION

The prevalence of feline sporotrichosis from January 2018 to December 2022 in University Veterinary Hospital (UVH), Universiti Putra Malaysia (UPM) was 1%. There was no previous study done on the prevalence of feline sporotrichosis in UVH. However, a similar study was conducted at Veterinary Medicine Teaching Hospital, Universiti Malaysia Kelantan (UMK) by Kosheilasri *et. al* (2023), revealing a higher prevalence of feline sporotrichosis at 1.70% (140 feline sporotrichosis cases / 8236 cats presented) from 2017 to 2022.

Furthermore, the trends of feline sporotrichosis cases presented at UVH from 2018 to 2022 illustrated the lowest number in the year 2020 which could be explained by the implementation of the Movement Control Order (MCO) which started on 18 March 2020 due to the COVID-19 pandemic in Malaysia. When combined with data from Chan *et al.* (2013) and Lee *et al.* (2018), the trend of feline sporotrichosis cases at UVH saw an increment from 2008 (n=24) and peaked in 2015 (n=164). Subsequently, there was a consistent reduction in the number of cases from the year of 2016 (n=108) to 2022 (n=37) (Chan *et al.*, 2013; Lee *et al.*, 2018). The decline in the number of cases could be attributed to the higher portion of second opinion and referral cases.

The median age of cats with feline sporotrichosis in UVH was 2 years old which was in accordance with results from previous studies (Schubach *et al.*, 2004; Chan *et al.*, 2013; Lee *et al.*, 2018). Intact, male and outdoor cats were found to have a higher number of sporotrichosis cases according to this study. This was likely because intact male cats that roam outdoors have a higher probability of fighting with other cats which makes them susceptible to puncture wounds that offer an advantageous route of transmission of sporotrichosis to the body (Alvarez *et al.*,

2022). Furthermore, outdoor cats have higher exposure to the environment, specifically the soil and the surface of the plants where *Sporothrix* spp. can naturally be found (Ramírez-Soto *et al.*, 2018). Despite being found to be the most common breed contracting feline sporotrichosis in this study, there is no proper research stating the predisposition of Domestic Shorthair breed toward feline sporotrichosis.

In various studies, the most common types of skin lesions are reported as ulcers and nodules, usually found on the head, nasal mucosa, extremities, and paws (Schubach *et al.*, 2004; Gremião *et al.*, 2015; Duangkaew *et al.*, 2019). Our results found that ulcerative lesion was the most common type of lesion which would often be found mainly on the nose (20.2%), followed by ears (11.7%), hindlimb (10.2%) and forelimb (9.9%). Previous retrospective studies done by Chan *et al.* (2013) and Lee *et al.* (2018) also affirmed this finding despite slight differences in the skin lesion distribution. The study by Lee *et al.* (2018) combining results from a previous study done by Chan *et al.* (2013) stated that skin lesion was mainly distributed on the forelimb (18%), nose (16%), hindlimb (15%) and ear (12%).

In addition to cutaneous lesions, this study also found involvement of extracutaneous signs, consisting of respiratory signs (n=57) and lymphadenopathy (n=49). This finding is consistent with research from Schubach *et al.* (2014), stating that respiratory signs were the most frequent extracutaneous signs observed in 44.4% of 347 cats infected with sporotrichosis. With sneezing recorded to be the highest number in this study (n=23), there is a concern about it being the potential route of transmission of sporotrichosis which will facilitate a higher rate of transmission compared to physical contact or fighting. Based on research by Bastos *et al.* (2022), cats infected with feline sporotrichosis can sneeze, releasing droplets containing viable *Sporothrix* yeast that is capable of infecting other animals and humans upon

mucosal exposure. Hence, cat owners and clinicians should always take the necessary precautions to prevent potential spread of sporotrichosis by wearing mask, glove and proper disinfection. Interestingly, submandibular lymph nodes enlargement demonstrated the highest number (n=32) in cases with lymphadenopathy. This is because submandibular lymph nodes provide drainage to most regions of the head which correlates with the distribution of lesions on the ears (11.7%) and the nose (20.2%) of cat with feline sporotrichosis in this study.

Cytology by impression smear was the most preferred method of diagnosis of feline sporotrichosis by the clinicians at UVH because the result was rapid with a sensitivity that ranged from 79% to 84.9% (Pereira *et al.*, 2011; Jessica *et al.*, 2015). Nevertheless, a definitive diagnosis can be achieved by performing a fungal culture and observing the morphology of the colony which can take around 1 month for the results. While cytology by impression smear has been widely used, it cannot distinguish between *Sporothrix* spp. and *Histoplasma* spp., despite both having similar treatment regimes. (Rodrigues *et al.*, 2022). Therefore, PCR has been explored as a valuable tool for the diagnosis of feline sporotrichosis, offering high sensitivity and specificity, and enabling the rapid identification of pathogenic *Sporothrix* spp., which is critical for early treatment and reducing the risk of zoonotic transmission (Leal *et al.*, 2022).

Itraconazole is currently considered the antifungal drug of choice in UVH for the treatment of sporotrichosis in cats because of its higher effectiveness and safety compared with other antifungal drugs (Welsh *et al.* 2003; Kauffman *et al.* 2007; Pereira *et al.* 2009; Pereira *et al.* 2010). The dosage of itraconazole used in UVH was 10 mg/kg daily, orally, until one month upon clinical cure. Nonetheless, testing liver parameters are crucial when itraconazole is prescribed for a protracted period to

avoid adverse effects on the liver function. Studies on the effectiveness and adverse effects of itraconazole and ketoconazole were conducted by Pereira *et al.* (2010) demonstrated that itraconazole had a higher clinical cure rate (38.3%) compared to ketoconazole (28.6%). The clinical cure rate was 1.3 times higher in the group of cats treated with itraconazole with a median treatment time that was 2 weeks shorter than ketoconazole (28 weeks).

Despite having itraconazole as the active ingredient, the generic drug Inox® and brand-name drug Sporanox® differ vastly in price. This led to the owners choosing Inox® as the antifungal medication as it is more affordable. However, clinicians would prefer to prescribe Sporanox® as they observed better recovery with this brand-name drug. Contrary to common clinicians' observation, a study by Renschler *et al.* (2018) shows that mean serum or plasma itraconazole concentration was within the therapeutic range for both the generic and brand name groups (Renschler, 2018). This suggests that both generic and brand-name drugs can deliver similar effect against the infection.

The median clinical cure time for feline sporotrichosis varies from a few weeks to several months, with different studies reporting median treatment durations ranging from 4 to 9 months (Gremião *et al.*, 2015; Gremião *et al.*, 2022; Rodrigues *et al.*, 2022). The duration of treatment may vary depending on whether there is a concurrent bacterial infection or systemic manifestation of the infection. The prognosis is usually good, if treatment duration and owner compliance are adequate (Welsh, 2003).

6.0 CONCLUSION

The prevalence of feline sporotrichosis diagnosed at UVH was 1% in the 5-year period of 2018 to 2022. Compared to the previous decade, there had been a noticeable reduction in feline sporotrichosis cases diagnosed at UVH from 2018 to 2022. The Domestic Shorthair breed was predominant, accounting for 80% of cases, with males making up 61% of the affected cats. Additionally, 29% of these cats were free roamers, and the median age was 2 years. Besides, the ulcerated wound was the most common type of lesion for feline sporotrichosis which was typically distributed on the nose, ear, hindlimb and forelimb. The commonly used antifungal therapy was itraconazole (99%) which was almost all the cases. Upon descriptive analysis of the cases recorded as recovered, the median recovery time was 68 days. Client education and awareness of proper treatment regimes and zoonotic risk are important in handling feline sporotrichosis cases.

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