

SHORT COMMUNICATION

Sporotrichosis: An Update on Epidemiology and In Vitro Antifungal Susceptibilities of *Sporothrix schenckii* Isolated From Humans and Cats in Klang Valley, Malaysia

Gayathri Thevi Selvarajah^{1,2}, Jacinta Santhanam³, Elizebeth Mah³, Jasper Elvin James⁴, Mohd Fuat Abdul Razak⁵, Raja Rajeswari Selvakumar³, Muhanna M. Al-shaibani³

¹ Department of Veterinary Clinical Studies, Faculty of Veterinary Medicine, Universiti Putra Malaysia, 43400 Serdang, Selangor, Malaysia.

² University Veterinary Hospital, Universiti Putra Malaysia, 43400 Serdang, Selangor, Malaysia.

³ Center for Toxicology and Health Risk Studies, Faculty of Health Sciences, Universiti Kebangsaan Malaysia, 50300 Kuala Lumpur, W. P. Kuala Lumpur, Malaysia.

⁴ Department of Biological Sciences and Biotechnology, Faculty of Science and Technology, Universiti Kebangsaan Malaysia, 43600 Bangi, Selangor, Malaysia.

⁵ Bacteriology Unit, Institute for Medical Research, Jalan Pahang, 50588 Kuala Lumpur, W. P. Kuala Lumpur, Malaysia

ABSTRACT

The epidemiological pattern of human sporotrichosis infections in Klang Valley, Malaysia and antifungal susceptibility of the causative fungal pathogen, *Sporothrix schenckii* was determined. A total of 67 culture positive sporotrichosis cases were recorded from 2015-2018 at three Klang Valley hospitals, with a majority in the 19-30 years age group. Association with felines represent the highest (47.76%) risk factor for sporotrichosis. The clinical presentation was predominantly lymphocutaneous infection (59.67%). *S. schenckii* isolates from humans and cats were tested for antifungal susceptibility using the standardized broth microdilution method. All 25 *S. schenckii* isolates tested were susceptible to itraconazole (MIC 0.5-2 µg/mL), while MIC was lower for ravuconazole (0.125-1 µg/mL). Awareness and emphasis on feline associated sporotrichosis are needed in Malaysia. While itraconazole is the recommended treatment, ravuconazole may be an additional, potentially effective treatment against *S. schenckii*. *Malaysian Journal of Medicine and Health Sciences* (2024) 20(4): 375-384. doi:10.47836/mjmhs20.4.45

Keywords: Sporotrichosis, *Sporothrix schenckii*, Malaysia, Itraconazole, Ravuconazole.

Corresponding Author:

Jacinta Santhanam, PhD

Email: jacinta@ukm.edu.my

INTRODUCTION

In recent years, sporotrichosis caused by *Sporothrix schenckii* has become an emergent disease worldwide. *S. schenckii* is globally distributed but more prevalent in tropical or subtropical (25-28 °C) regions [1]. Sporotrichosis infections are commonly caused by inoculation of the fungus into the skin or mucous membrane. Zoonotic and environmental transmission most commonly occur, as the fungus is present in soil or plant material and feline infections are frequently reported [1]. The high fungal load in skin lesions of cats [2] and the presence of the fungus in their claws and oral

cavity have contributed to human sporotrichosis [3]. Due to the high prevalence of cats as domestic pets living in close proximity with owners, it is not unexpected that cat-related infections occur more frequently in urban areas.

While the incidence of sporotrichosis has been acknowledged worldwide and an increasing trend of infections was inferred in Malaysia [4], the national data on epidemiology of human infections and susceptibility of *Sporothrix* isolates is very limited. We aimed to determine the sociodemographic factors and the prevalent clinical presentation for sporotrichosis in Klang Valley, an area in Malaysia that includes Kuala Lumpur and its adjoining cities and towns in the state of Selangor. In addition, we evaluated itraconazole and ravuconazole susceptibilities of *Sporothrix schenckii* isolates from humans and cats.

MATERIAL AND METHOD

Ethics approval

Ethics approval was obtained from the Medical Research and Ethics Committee (MREC), Ministry of Health Malaysia to obtain data on epidemiology of human sporotrichosis infection in Klang Valley and was registered with the National Medical Research Register (NMRR; registration no: NMRR-18-2910-42880).

Data collection of human sporotrichosis cases

Data from 2015 to 2018 were analysed for the epidemiology study. The three hospitals that participated in this study were: Hospital Kuala Lumpur (HKL) with 2,300 beds, Hospital Sungai Buloh (HSB) with 620 beds and Hospital Tengku Ampuan Rahimah Klang (HTAR) with 1,094 beds. Data were retrieved from records of the hospitals’ microbiology laboratories which included the patients’ demography (age, gender, and occupation), exposure history, and laboratory diagnosis method.

Antifungal susceptibility testing of *Sporothrix* isolates

A total of 25 *S. schenckii* sensu stricto isolates from cats and humans tested for their antifungal susceptibilities in this study were identified using their calmodulin sequences in our previous report [4]. The six isolates from cats were collected from the University Veterinary Hospital at Universiti Putra Malaysia while the 19 human isolates were obtained from the Institute for Medical Research, Kuala Lumpur. Antifungal susceptibility testing against itraconazole (ITC) and ravuconazole (RVC) (Sigma, St Louis, MO, USA) was carried out according to the standardized CLSI M38-A2 broth microdilution protocol [5]. The microtiter plates with mycelial phase fungal inoculums and antifungal agent in triplicates were incubated for 72 hours at 35 °C. Minimum inhibitory concentration was determined at 100% growth inhibition.

RESULTS AND DISCUSSION

Patients’ distribution: gender and age

There was a total of 67 culture-confirmed human sporotrichosis cases reported for the years 2015 to 2018, from HKL, HTAR and HSB. The gender distribution was comparable with 50.75% female (n = 34) and 49.25% male (n = 33) patients. The median age of sporotrichosis patients was 42 and the patients age ranged from 4-94 years old. The majority of sporotrichosis patients were in the age group of 19-30 years old (32.84%, n = 22), followed by patients above 61 years old (26.87%, n = 18). Ten patients (14.93%) were aged 51-60, another 10 were 31-50 years old while 6 (8.96%) were below 18 years old. The age of one patient from HKL was unknown. There was limited information available for occupation of patients, therefore this data was excluded.

Sporotrichosis exposure

The possible sources of infection for human

sporotrichosis were divided into four categories based on patients’ history: contact with cat, environment-related, unknown, and others (Figure 1). For cat-related cases, patients had direct contact with cats i.e., house cats, had contact with stray cats, or had history of being scratched or bitten by cats. The cats of three patients in this study were diagnosed with feline sporotrichosis. Cases with a history of gardening or agricultural activities were categorized as environment related. Three cases categorised as “others” reported no exposure to cats or environmental-related activities. Furthermore, 28 patients were categorised under the “unknown” category (41.79%) due to not being able to identify the possible source of infection, or unavailability of data from patient records. Cat-related cases topped the list of human sporotrichosis in this study (47.76%, n = 32) and felines are likely the major transmission source for all age groups when the “unknown” category is excluded. The environment-related cause accounted for only 5.97% (n = 4) of cases. The patients in this category were all above 41 years old and included history of body parts being pricked by plant thorns and palm leaves while gardening.

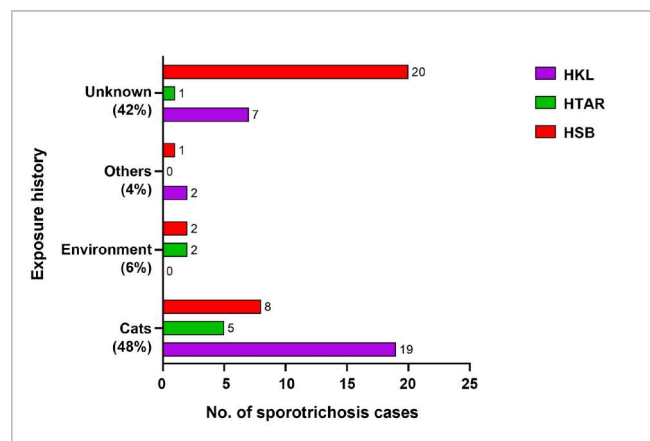


Figure 1: The number of human sporotrichosis cases (2015-2018) categorised according to exposure history from data collected at Hospital Kuala Lumpur (HKL), Hospital Tengku Ampuan Rahimah Klang (HTAR) and Hospital Sungai Buloh (HSB).

Feline associated sporotrichosis

In Malaysia, previous studies on human sporotrichosis were small scale and case-specific which involved 19 cases of cutaneous sporotrichosis between July, 2004 to June, 2010 (six-year study) at HKL [6]. Another study at Hospital Raja Permaisuri Bainun, Ipoh, reported 51 patients diagnosed with cutaneous sporotrichosis from January 2011 to August 2015 [7]. A review of these previous findings and our data suggests that human sporotrichosis infection in Malaysia is increasing and felines as an important disease transmission source. A limitation in the present study is that only culture proven sporotrichosis cases were documented, therefore the actual number of cases may be higher.

Clinical presentation in patients

The clinical manifestation of cutaneous sporotrichosis

ranged from single (fixed cutaneous) to multiple lesions (lymphocutaneous) to disseminated infection (Table I). Lymphocutaneous infection was the most common presentation (59.67%), followed by fixed cutaneous (32.25%). Disseminated cutaneous sporotrichosis was observed in three patients, two of whom were immunocompromised. The health status of the third

patient was unknown. Two immunocompromised patients had systemic infections without apparent skin lesions, where the fungus was isolated from blood culture. Itraconazole was most often prescribed as it is the primary treatment option. These clinical findings are similar to a previous report from Malaysia [7].

Table I : Sociodemographic factors, exposure history, health status, clinical presentation, laboratory diagnosis results and treatment prescribed for sporotrichosis patients at HSB, HKL and HTAR from 2015 to 2018.

Patient No.	Study site	Sex	Age	Exposure history	Health status	Clinical presentation	Sample for culture	Laboratory diagnosis	Treatment
1	HSB	M	80	NA	Immuno-compromised	Fever, cough, headache, no skin lesions.	Blood - Myco F/lytic	Culture & microscopy - <i>Sporothrix schenckii</i>	Augmentin, azithromycin
2	HSB	M	29	NA	Immuno-compromised	Multiple lesions; vesicles on abdomen, right arm, left thigh.	Tissue	Culture & microscopy - <i>Sporothrix schenckii</i>	Fluconazole
3	HSB	M	71	NA	NA	NA	Tissue	Culture & microscopy - <i>Sporothrix schenckii</i>	NA
4	HSB	M	27	NA	NA	Multiple lesions over face	Skin	Culture & microscopy - <i>Sporothrix schenckii</i>	Itraconazole
5	HSB	M	67	Environment; pricked by palm tree leaf	NA	Initial injury on left index finger, pus & discharge, subsequent multiple lesions on wrist, forearm, arm.	Tissue	Culture & microscopy - <i>Sporothrix schenckii</i>	Itraconazole
6	HSB	M	73	Cat	NA	Verrucose plaque on dorsum of left big toe, swelling over left foot.	Tissue	Culture & microscopy - <i>Sporothrix schenckii</i>	Itraconazole
7	HSB	M	30	NA	Immuno-compromised	Single skin lesion on left arm, with pus discharge and fever.	Tissue	Culture & microscopy - <i>Sporothrix schenckii</i>	Fluconazole, itraconazole
8	HSB	F	35	Cat	NA	Multiple lymphocutaneous lesions on right hand and right thumb.	Tissue	Culture & microscopy - <i>Sporothrix schenckii</i>	Cloxacillin, itraconazole
9	HSB	M	46	NA	NA	Multiple lesions with swelling over left upper limb, over proximal aspect of arm.	Tissue	Culture & microscopy - <i>Sporothrix schenckii</i>	Itraconazole
10	HSB	F	54	NA	NA	Multiple lymphocutaneous lesions; tender nodules at left hand extending to left forearm.	Tissue	Culture & microscopy - <i>Sporothrix schenckii</i>	Itraconazole
11	HSB	F	29	Cat	NA	Multiple lesions; papules on dorsum of right hand and base of right index finger.	Tissue	Culture & microscopy - <i>Sporothrix schenckii</i>	Itraconazole
12	HSB	M	47	Environment; handled palm leaves	NA	Multiple subcutaneous lesions over right hand.	Tissue	Culture & microscopy - <i>Sporothrix schenckii</i>	Itraconazole

CONTINUE

Table 1 : Sociodemographic factors, exposure history, health status, clinical presentation, laboratory diagnosis results and treatment prescribed for sporotrichosis patients at HSB, HKL and HTAR from 2015 to 2018. (CONT.)

Patient No.	Study site	Sex	Age	Exposure history	Health status	Clinical presentation	Sample for culture	Laboratory diagnosis	Treatment
13	HSB	M	28	NA	Immuno-compromised	Unwell and unable to walk.	Blood - Myco F/Lytic	Culture & microscopy - <i>Sporothrix schenckii</i>	Tazocin, amphotericin
14	HSB	F	78	NA	NA	Non-healing ulcer over right hand, single lesion.	Tissue	Culture & microscopy - <i>Sporothrix schenckii</i>	Itraconazole, miconazole
15	HSB	F	27	Cat	NA	Single lesion on right index finger.	Tissue	Culture & microscopy - <i>Sporothrix schenckii</i>	Augmentin, itraconazole
16	HSB	M	66	NA	Immuno-compromised	Multiple lesions; erythematous nodules along dorsum of hands extending to right forearm and arm.	Tissue	Culture & microscopy - <i>Sporothrix schenckii</i>	Itraconazole, cloxacillin, erythromycin
17	HSB	F	94	NA	NA	Multiple lymphocutaneous lesions; nodules over right upper limb, erythema of right index finger.	Tissue	Culture & microscopy - <i>Sporothrix schenckii</i>	Itraconazole
18	HSB	M	19	Cat; scratched by cats	NA	Multiple lymphocutaneous lesions; nodules over left arm.	Tissue	Culture & microscopy - <i>Sporothrix schenckii</i>	Itraconazole
19	HSB	M	65	NA	NA	Multiple lymphocutaneous lesions; itchy, erythematous nodules at exterior aspects of left forearm.	Tissue	Culture & microscopy - <i>Sporothrix schenckii</i>	Augmentin, itraconazole
20	HSB	M	57	NA	NA	Itchy rash over limbs and buttocks, blackish discoloration of right thumb, with partially avulsed nail.	Nail Scraping	Culture & microscopy - <i>Sporothrix schenckii</i>	NA
21	HSB	F	16	NA	Immuno-competent	Single lesion on left cheek, with swelling.	Tissue	Culture & microscopy - <i>Sporothrix schenckii</i>	Itraconazole
22	HSB	M	25	NA	Immuno-compromised	Disseminated cutaneous lesions, with fever, chills, odynophagia, joint pain.	Tissue, Blood	Culture & microscopy - <i>Sporothrix schenckii</i>	Fluconazole, itraconazole, amphotericin
23	HSB	M	30	NA	Immuno-compromised	Disseminated cutaneous, lesions, started with vesicles on right anterior chest with itching and yellowish discharge, subsequent spread all over body.	Skin	Culture & microscopy - <i>Sporothrix schenckii</i>	Fluconazole, acyclovir, amphotericin

CONTINUE

Table I : Sociodemographic factors, exposure history, health status, clinical presentation, laboratory diagnosis results and treatment prescribed for sporotrichosis patients at HSB, HKL and HTAR from 2015 to 2018.(CONT.)

Patient No.	Study site	Sex	Age	Exposure history	Health status	Clinical presentation	Sample for culture	Laboratory diagnosis	Treatment
24	HSB	F	68	NA	Immuno-compromised	Swelling over left cheek.	Tissue	Culture & microscopy - <i>Sporothrix schenckii</i>	Itraconazole
25	HSB	M	4	NA	NA	Multiple lesions on left hand, started with nodule then pus discharge.	Tissue	Culture & microscopy - <i>Sporothrix schenckii</i>	Itraconazole, miconazole, ketoconazole
26	HSB	F	73	NA	NA	Multiple lesions over left cheek, ulcerated.	Tissue	Culture & microscopy - <i>Sporothrix schenckii</i>	Erythromycin ethylsuccinate, itraconazole
27	HSB	M	21	NA	NA	Multiple lesions with pain (pricking nature) over left ankle.	Tissue	Culture & microscopy - <i>Sporothrix schenckii</i>	Augmentin, itraconazole, erythromycin ethylsuccinate
28	HSB	M	69	NA	NA	Multiple scaly lesions over both feet.	Skin	Culture & microscopy - <i>Sporothrix schenckii</i>	Miconazole, clotrimazole
29	HSB	F	53	Cat	NA	Multiple lesions; itchy rash over axillary and inframmary fold.	Skin	Culture & microscopy - <i>Sporothrix schenckii</i>	Cloxacillin, itraconazole, ketoconazole, miconazole
30	HSB	M	26	Cat	NA	Multiple lesions with itch and pain, presence of wound over the back.	Tissue	Culture & microscopy - <i>Sporothrix schenckii</i>	Itraconazole, augmentin
31	HSB	M	12	Cat	NA	Multiple lesions.	Skin	Culture & microscopy - <i>Sporothrix schenckii</i>	Miconazole, ketoconazole, aqueous cream, betnovate, griseofulvin
32	HKL	M	68	Cat	NA	Multiple nodules, maculopapular rashes.	Skin	Culture & microscopy - <i>Sporothrix schenckii</i>	NA
33	HKL	M	74	Cat	NA	Multiple erythematous papules with minimal pus.	Skin	Culture & microscopy - <i>Sporothrix schenckii</i> with few pus cells	NA
34	HKL	F	59	Cat	Hypertension, bronchiol asthma, allergic rhinitis	Single lesion; solitary erythematous plaque over left arm.	Skin	Culture & microscopy - <i>Sporothrix schenckii</i> with few pus cells	NA
35	HKL	F	21	Cat	NA	Single lesion; with intermittent pain, pus and hemoserous discharge.	Skin	Culture & microscopy - <i>Sporothrix schenckii</i>	NA

CONTINUE

Table 1 : Sociodemographic factors, exposure history, health status, clinical presentation, laboratory diagnosis results and treatment prescribed for sporotrichosis patients at HSB, HKL and HTAR from 2015 to 2018.(CONT.)

Patient No.	Study site	Sex	Age	Exposure history	Health status	Clinical presentation	Sample for culture	Laboratory diagnosis	Treatment
36	HKL	F	59	Cat	NA	Single lesion; erythematous nodular lesion at forearm.	Tissue	Culture & microscopy - <i>Sporothrix schenckii</i> with few pus cells	NA
37	HKL	F	45	NA	NA	Multiple lesions at right forearm.	Skin	Culture & microscopy - <i>Sporothrix schenckii</i>	NA
38	HKL	M	29	NA	NA	Single lesion; erythematous nodule at right upper limb.	Skin	Culture & microscopy - <i>Sporothrix schenckii</i>	NA
39	HKL	F	23	Cat	NA	Single lesion; solitary nodule at right wrist with pus discharge.	Skin	Culture & microscopy - <i>Sporothrix schenckii</i>	NA
40	HKL	F	50	Cat	NA	Multiple painful, erythematous nodules on left second finger.	Skin	Culture & microscopy - <i>Sporothrix schenckii</i>	NA
41	HKL	F	82	NA	NA	Multiple lesions; abrasion wound at right ankle with cellulitis, nodules at the right ankle and right medial thigh.	Skin	Culture & microscopy - <i>Sporothrix schenckii</i>	Cloxacillin
42	HKL	F	35	Cat	Breast cancer	Single lesion; non healing ulcerated wound at dorsum of wrist.	Skin	Culture & microscopy - <i>Sporothrix schenckii</i>	NA
43	HKL	F	40	NA	NA	Multiple nodules at right arm, ulcerated with pus and bloody discharge.	Skin	Culture & microscopy - <i>Sporothrix schenckii</i> with few pus cells	NA
44	HKL	F	30	NA	NA	Multiple lesions; bilateral lower limb swelling, erythematous nodules on left elbow, ulcerated with serous discharge.	Skin	Culture & microscopy - <i>Sporothrix schenckii</i>	NA
45	HKL	F	26	Cat diagnosed with sporotrichosis	NA	Multiple nodules, abscess ascending along lymph tract.	Skin	Culture & microscopy - <i>Sporothrix schenckii</i> with few pus cells	NA
46	HKL	F	56	Cat	NA	Multiple lesions; granulomatous lesions on extensor at right wrist and cheek.	Skin	Culture & microscopy - <i>Sporothrix schenckii</i>	Neomycin
47	HKL	F	28	Cat and environment	Blister over left middle finger and pus discharge due to hot oil.	Multiple, tender nodules in lymphatic distribution on left hand to forearm.	Skin	Culture & microscopy - <i>Sporothrix schenckii</i> with few pus cells	Doxycyclin, augmentin, cefuroxime, flagyl (metronidazole)

CONTINUE

Table I : Sociodemographic factors, exposure history, health status, clinical presentation, laboratory diagnosis results and treatment prescribed for sporotrichosis patients at HSB, HKL and HTAR from 2015 to 2018.(CONT.)

Patient No.	Study site	Sex	Age	Exposure history	Health status	Clinical presentation	Sample for culture	Laboratory diagnosis	Treatment
48	HKL	M	5	Cat	NA	Multiple nodules, ulcer at distal dorsum of right hand, two nodules at forearm and arm.	Skin	Culture & microscopy - <i>Sporothrix schenckii</i>	NA
49	HKL	F	NA	Cat; cat bite	Hypertension	Multiple lesions; right hand abscess, pus discharge, formed multiple new lesions on right forearm with fever.	Skin	Culture & microscopy - <i>Sporothrix schenckii</i> with few pus cells	NA
50	HKL	M	33	NA	Immunocompromised; RVD on HAART, Hepatitis C, adrenal insufficiency, <i>Mycobacterium avium</i>	Generalized skin changes and desquamation.	Nail	Culture & microscopy - <i>Sporothrix schenckii</i>	NA
51	HKL	M	66	Cat with mucosal infection	NA	Multiple painful nodules at left forearm, initially from index finger then spread to arm.	Skin	Culture & microscopy - <i>Sporothrix schenckii</i> with few pus cells	NA
52	HKL	M	58	NA	NA	NA	Skin	Culture & microscopy - <i>Sporothrix schenckii</i>	Itraconazole, miconazole
53	HKL	F	34	Cat	Chicken pox in previous month.	Single lesion; excoriation, painful and itchy erythema developed over right hand with pus discharge.	Skin	Culture & microscopy - <i>Sporothrix schenckii</i>	NA
54	HKL	M	25	NA	NA	Left wrist abscess.	Skin	Culture & microscopy - <i>Sporothrix schenckii</i>	NA
55	HKL	F	62	Cat; cat scratch	NA	Multiple nodules; erythematous plaques with central papule dorsum, nodules on dorsum of right hand, with pus discharge.	Skin	Culture & microscopy - <i>Sporothrix schenckii</i>	NA
56	HKL	F	29	Cat diagnosed with sporotrichosis; cat scratch	NA	Multiple lesions; pustules over left wrist with nodules on left forearm.	Skin	Culture & microscopy - <i>Sporothrix schenckii</i>	NA
57	HKL	M	58	NA	NA	Single lesion; verrucous lesion on left leg.	Tissue	Culture & microscopy - <i>Sporothrix schenckii</i>	Cefuroxime
58	HKL	F	44	Cat; cat scratch	NA	Multiple lesions; painful erythematous rash on left thumb with erythematous nodules on left forearm.	Skin	Culture & microscopy - <i>Sporothrix schenckii</i>	NA

CONTINUE

Table 1 : Sociodemographic factors, exposure history, health status, clinical presentation, laboratory diagnosis results and treatment prescribed for sporotrichosis patients at HSB, HKL and HTAR from 2015 to 2018.(CONT.)

Patient No.	Study site	Sex	Age	Exposure history	Health status	Clinical presentation	Sample for culture	Laboratory diagnosis	Treatment
59	HKL	M	29	Cat	NA	Disseminated; multiple erythematous plaque and papules on face, neck, chest and abdomen.	Skin	Culture & microscopy - <i>Sporothrix schenckii</i> with few pus cells	NA
60	HTAR	F	61	Cat	NA	Single lesion; nodular lesion on left wrist.	Skin	Culture & microscopy - <i>Sporothrix schenckii</i>	Itraconazole
61	HTAR	F	67	Cat	NA	Single lesion over dorsum of left hand.	Skin	Culture & microscopy - <i>Sporothrix schenckii</i> , HPE- chronic granulomatous inflammation	Itraconazole
62	HTAR	F	22	NA	NA	Mutiple nodules over left arm.	Skin	Culture & microscopy - <i>Sporothrix schenckii</i>	Itraconazole
63	HTAR	M	16	Cat	NA	Single lesion; ulcerated nodule at extensor left forearm.	Skin	Culture & microscopy - <i>Sporothrix schenckii</i> , HPE- dermatitis due to fungal infection	Itraconazole
64	HTAR	M	70	Environment; gardening	NA	Mutiple nodular lesions over left index finger.	Punch	Culture & microscopy - <i>Sporothrix schenckii</i> , HPE- suppurative granulomatous inflammation compatible with sporothricosis	Itraconazole
65	HTAR	F	21	Cat	NA	Single lesion; nodule over right wrist (dorsal aspect).	Skin	Culture & microscopy - <i>Sporothrix schenckii</i> , HPE- necrotising granulomatous inflammation	Itraconazole
66	HTAR	F	57	Cat	NA	Single nodular lesion over right forearm.	Skin	Culture & microscopy - <i>Sporothrix schenckii</i> , HPE- necrotising granulomatous inflammation	Itraconazole
67	HTAR	M	53	Environment	NA	Persistent rashes over bilateral upper limbs.	Skin	Culture & microscopy - <i>Sporothrix schenckii</i> , HPE- chronic granulomatous inflammation	NA

HSB, Hospital Sungai Buloh, HKL, Hospital Kuala Lumpur, HTAR, Hospital Tuanku Ampuan Rahimah; NA, not available; HPE, histopathological examination.

Antifungal susceptibility profile of *Sporothrix* isolates

Our results revealed that RVC was the more active drug, showing an MIC range of 0.125-1 µg/mL and geometric mean (GM) of 0.39 µg/mL, compared to ITC which had higher MIC range of 0.5-2 µg/mL and a GM value of 1.21 µg/mL (Table II). The MIC values for itraconazole were within the epidemiological cutoff values (ECV; 2 µg/mL) for *Sporothrix schenckii* [8] which indicated that none of the isolates were resistant to ITC.

Table II. MIC values of itraconazole and ravuconazole against 25 *S. schenckii* sensu stricto isolates from humans (n = 19) and cats (n = 6).

Isolate no.	Source ^a	MIC (µg/mL)	
		Ravuco- nazole	Itraconazole
MYSsH1	Human*	1.0	2.0
MYSsH2	Human	0.125	0.5
MYSsH3	Human*	0.25	1.0
MYSsH4	Human	1.0	2.0
MYSsH5	Human*	1.0	2.0
MYSsH6	Human	0.25	1.0
MYSsH7	Human	0.25	1.0
MYSsH8	Human	1.0	2.0
MYSsH9	Human	0.25	0.5
MYSsH10	Human	0.25	2.0
MYSsH11	Human*	0.25	1.0
MYSsH12	Human	1.0	2.0
MYSsH13	Human	0.5	1.0
MYSsH14	Human	0.25	1.0
MYSsH15	Human*	0.5	1.0
MYSsH16	Human*	0.25	1.0
MYSsH17	Human	0.25	1.0
MYSsH18	Human*	1.0	2.0
MYSsH19	Human	0.25	1.0
MYSsF1	Cat	1.0	2.0
MYSsF2	Cat	0.5	2.0
MYSsF3	Cat	0.25	1.0
MYSsF4	Cat	0.25	1.0
MYSsF5	Cat	0.25	1.0
MYSsF6	Cat	0.25	1.0
Quality control 1	<i>Candida krusei</i> ATCC 6258	0.016	0.0625
Quality control 2	<i>Candida parapsilosis</i> ATCC 22019	0.0625	1.0

^aAsterisk indicates patient with reported history of contact with cats.

ITC has been the primary treatment option for sporotrichosis [9] and in Rio de Janeiro, Brazil, ITC showed excellent therapeutic response in an evaluation of 645 patients with *S. schenckii* infection [10]. The ITC susceptibilities of *S. schenckii* isolates in our study is in agreement with a 2018 report in Mexico, where 38 isolates of *S. schenckii* showed ITC MIC range of 0.125-2 µg/mL [11]. Similarly, a previous study on 40 *S. schenckii* sensu stricto isolates from cats in Malaysia reported ITC MIC range of 0.5-2 µg/mL for 38 isolates, and 4 µg/mL MIC for two isolates [12]. A recent Malaysian study [13] reported very low MIC values for ITC (GM 0.20 µg/ml) and RVC (GM 0.16 µg/ml). In contrast, high ITC, posaconazole, and amphotericin B MICs were reported for *S. schenckii* in Brazil [14], indicating a need for more effective antifungals for sporotrichosis treatment. Comparing the available antifungal susceptibility data for *S. schenckii* in Malaysia and Brazil may indicate that Malaysian isolates are still susceptible to itraconazole, which has been supported by in vivo data in humans [7, 15], while in cats the prognosis may be poor with a higher dose of ITC required for unresponsive cases [16]. The RVC MIC of the *S. schenckii* sensu stricto isolates in our study is between two to eight times lower than ITC MIC. In contrast, 59 *S. schenckii* isolates from cat-transmitted sporotrichosis epidemic in Rio de Janeiro, Brazil showed an MIC₉₀ = 4 µg/mL, however, the specific molecular identity within the *S. schenckii* complex was not determined [17]. To date, data on RVC therapeutic activity against sporotrichosis is not yet available but promising activity has been reported in clinical trials for onychomycosis treatment [18, 19].

CONCLUSION

In summary, association with cats remains the major risk factor for human sporotrichosis. This study found that ITC and RVC exhibited excellent in vitro activity against *S. schenckii* sensu stricto isolates, with RVC being the more active triazole. Thus, we suggest that the use of RVC as an antifungal drug for the treatment of sporotrichosis in humans and cats to be investigated further.

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