ORIGINAL ARTICLE

Epidemiology and Antifungal Susceptibility Profiling of Clinical Isolates From a Community Acquired Tinea Imbricata Outbreak Among the Bateq Subtribe in Pahang, Malaysia

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ABSTRACT

Introduction: Tinea imbricata (TI) outbreak poses a significant health burden among indigenous populations in rainforest regions due to their geographical isolation and poor socioeconomic conditions. This study aimed to investigate the epidemiological trends, antifungal susceptibility patterns, and treatment outcomes of TI among the Bateq subtribe in Pahang, Malaysia. **Materials and Methods:** A cross-sectional survey was conducted between July–October 2023 in five villages within the National Rainforest Park, Malaysia. Socio-demographic characteristics, clinical manifestations, and treatment outcomes were collected through interviews, laboratory investigations, and clinical examinations. Treatment modalities were evaluated for their effectiveness in reducing disease burden. **Results:** 569 individuals were surveyed, revealing a TI prevalence rate of 7.91% with children aged 15 years and below exhibiting the highest susceptibility (9.22%). Antifungal susceptibility testing of clinical isolates of *Trichophyton concentricum* demonstrated high sensitivity to terbinafine (GM MIC=0.144 µg/ml, GM MFC=0.198 µg/ml, $p<0.05$) and griseofulvin (GM MIC=1.741 µg/ml, GM MFC=4.782 µg/ml, $p<0.05$), while clotrimazole showed moderate activity (GM MIC=5.897 µg/ml, GM MFC=22.291 µg/ml). Fluconazole demonstrated the least potency, with no fungicidal activity observed at concentrations up to 128 µg/ml. Treatment outcomes indicated that combination therapy (terbinafine gel and oral griseofulvin) significantly outperformed terbinafine gel alone, achieving an almost complete lesion resolution (LA reduced to 0.158±0.158 cm versus 3.684±1.522 cm , $p<0.05$). **Conclusion:** These findings provide critical insights into the epidemiology and emerging drug resistance of TI in the Bateq subtribe, highlighting the importance of continued surveillance, monitoring, and adaptation of treatment strategies to combat evolving antifungal resistance patterns.
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Keywords: Tinea imbricata (TI), *Trichophyton concentricum*, Antifungal susceptibility, Indigenous population, Bateq subtribe, Drug resistance.

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INTRODUCTION

Tinea imbricata (TI) is an uncommon superficial cutaneous mycosis caused by the anthropophilic dermatophyte *Trichophyton concentricum*. It is clinically characterized by distinctive concentric rings, annular or lamellar plaques with scaly borders on all parts of the skin of the affected body parts (1). Although globally sporadic, TI is endemic in specific regions, including parts of Southeast Asia (2), the Pacific Islands (3,4), and Southwest Asia (5), particularly within remote and indigenous populations (4,6). The disease significantly affects the quality of life due to persistent discomfort, disfigurement, and associated social stigma.

In an epidemiological context, an "outbreak" refers to the occurrence of disease cases exceeding the normally expected frequency within a defined community or geographic region during a specific timeframe (7). TI outbreaks have been documented sporadically within indigenous populations, driven by factors such as limited healthcare accessibility, poor medication adherence, cultural practices, and environmental conditions

favouring fungal transmission (4,6). In Malaysia, the prevalence of TI among indigenous communities has received limited scientific attention. A recent study by Er et al. (2024) reported that 7.5% Negrito communities were affected by TI, with 9.4% of cases occurring among those residing inland and 3.9% among those in resettled villages (8). Nonetheless, sporadic outbreaks of TI among the indigenous community residing in Kampung Kuala Koh, Gua Musang, Kelantan have been periodically reported in the news (9,10). Some individuals within these communities reported a prolonged untreated cutaneous TI infection due to the delay in recognition of the condition by treating healthcare providers and poor medication adherence and follow-up. A study conducted two decades ago in 2002, revealed that from 1993 to 2000, 20 cases of TI were diagnosed at University of Malaya Medical Centre (UMMC) among indigenous individuals (11). A recent case study revealed the persistent nature of this disease within indigenous populations, particularly among isolated subgroups such as the Bateq subtribe in Peninsular Malaysia (12).

Along with efforts to address the persistent outbreaks of TI among indigenous communities, it is also vital to tackle the concern of emerging antifungal drug resistance (13). To date, there has been an epidemic increase in resistance among cutaneous dermatophyte infections, including TI, to commonly prescribed antifungal drugs such as terbinafine (14), itraconazole (15), and clotrimazole (16). Recently, fluconazole has also been reported to exhibit reduced susceptibility in treating dermatophytosis (17,18). The emergence of resistance may stem from various factors, including the inappropriate use of antifungals with corticosteroid drugs (17), non-adherence to prescribed medication regimens, the improper application of topical antifungal drugs, which can be easily wiped off (19), and environmental influences. These findings highlight the urgent need for vigilant antimicrobial stewardship practices to address the growing challenge of antifungal resistance in dermatophyte infections. Consequently, healthcare practitioners must possess a thorough understanding of prevalent dermatological conditions within indigenous populations to ensure accurate diagnosis and the implementation of effective treatment protocols. Hence, we aim to investigate the epidemiological patterns of a community-acquired outbreak of TI among the Bateq subtribe in Pahang, Malaysia. Additionally, the study seeks to evaluate the effectiveness of treatment strategies in controlling the spread of the disease, mitigating the potential emergence and spread of antifungal drug resistance, and improving health outcomes within these communities.

MATERIALS AND METHODS

Study setting and sample population

This study was conducted from July to October 2023 within five villages situated in the National Rainforest Park of Pahang, Peninsular Malaysia. These villages, namely Becah Kelubi, Jeram Dedari, Kampung Ulu Sat, Sungai Garam, and Sungai Sekin, are inhabited by 569 indigenous individuals from the Bateq subtribe, making them the largest such population in Malaysia. These villages have a climate that is characterized by extreme tropical humidity throughout the year, with a mean annual temperature of 25.2 °C (77.36 °F) and mean annual precipitation of approximately 3999 mm (20).

Patients and clinical isolates

This study consisted of a multidisciplinary team composed of physicians, pharmacists, nurses, and researchers. During a general medical checkup, all individuals who presented with acute and chronic cutaneous lesions (n=45) were included in the study. Trained research personnel conducted face-to-face interviews with participants to collect socio-demographic information, including age, gender, way of life, hygiene practices, and household characteristics. Clinical examinations were performed to assess the presence, severity, and progression of TI lesions, as well as other relevant clinical manifestations.

Skin scrapings were collected from 45 patients presenting with characteristic signs of TI, such as widespread, multiple annular, concentric rings of pink-red scaly lesions with pruritus (Figure 1). These samples were obtained using a scalpel blade and were inoculated on-site onto Sabouraud's dextrose agar (SDA; Life Technologies, USA) supplemented with 0.5 g/l chloramphenicol (Sigma Aldrich, Germany) and 0.5 g/l cycloheximide (Merck Millipore, USA). The inoculated plates were transported and incubated at 30 °C for up to 4 weeks for laboratory confirmation of fungal infection.

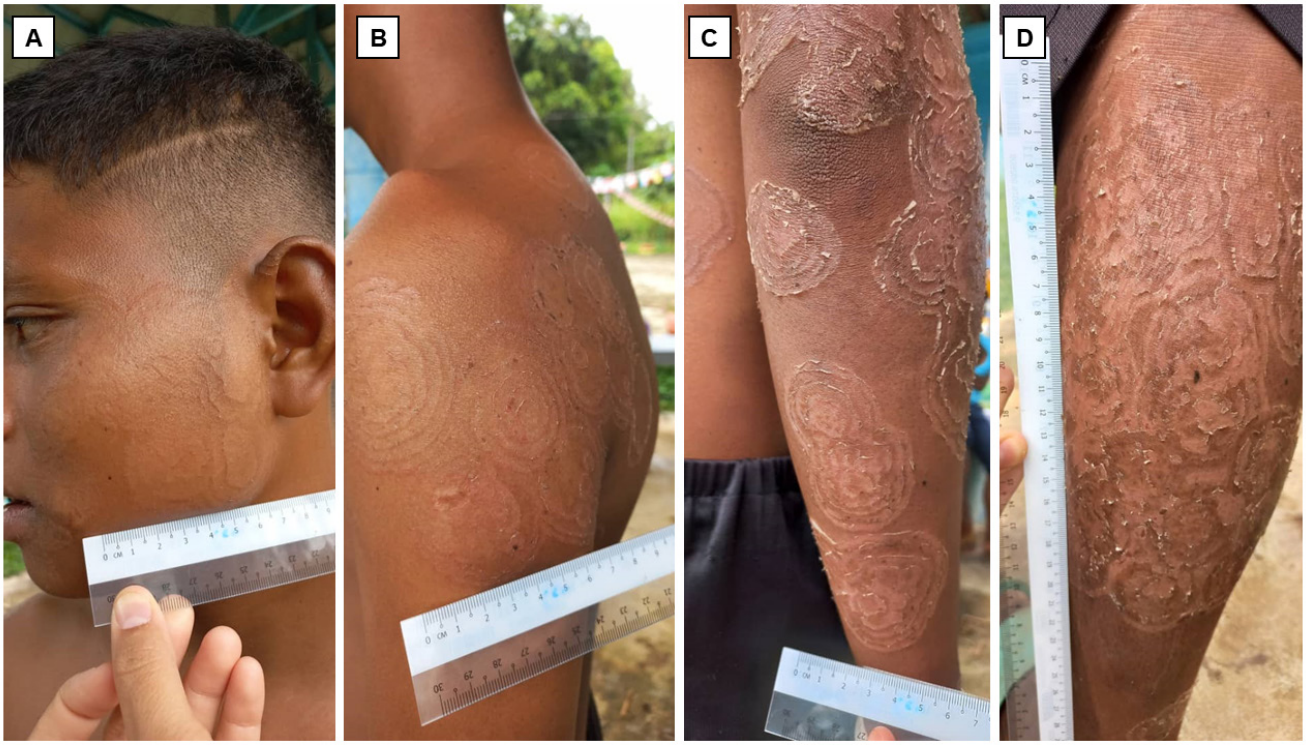

Figure 1: Clinical presentation of tinea imbricata patient. A 20-year-old male, showing characteristic concentric, imbricated rings with coarse and lamellar scales. Lesions affected multiple areas of the body, including (A) the face, (B) the shoulder and upper back, (C) the hand, and (D) the lower limb.

Antifungal susceptibility assay

The antifungal susceptibility of 45 *T. concentricum* clinical isolates was tested to detect potential resistance to major antifungal agents, following the Clinical Laboratory Standards Institute M38-A2 guidelines (21). To prepare conidia for testing, isolates were incubated on SDA at 30 °C for 7–10 days. Spores of the cultured strain were then gently collected by placing 10-ml sterilised 0.9% saline on top of colonies and aspirating the suspension into a sterile 15-ml centrifuge tube (Thermo Fisher Scientific, USA) and letting it settle for 15 minutes. The conidial suspension was adjusted to a final concentration of 1–4 x 106 conidia/ml. The broth microdilution method was performed using sterile and disposable 96-well U-shaped bottom microtiter plates (Corning, USA). The clinical isolates were subjected to various concentrations (0.0625–128 µg/mL) of antifungal drugs: terbinafine (HiMedia, India), griseofulvin (HiMedia, India), clotrimazole (HiMedia, India), and fluconazole (HiMedia, India). The minimal inhibitory concentration (MIC) assays were performed in triplicate, with Candida parapsilosis (ATCC®—22019) and *C. krusei* (ATCC®—14243) were used as quality controls.

In brief, 100 µL of antifungal drugs were serially diluted in RPMI 1640 (Life Technologies, USA) that was buffered with 0.165 M of morpholine-propane sulfonic acid (MOPS; Sigma Aldrich, Germany) at pH 7.0 and discarded at the end of each well (22). Subsequently, 100 µL of the prepared conidial suspension was added in each test well, excluding the sterility control wells. The 96-well plates were then incubated for 4–7 days at 30 °C. The MIC50, MIC90, and geometric mean (GM) MIC were established in accordance with the guidelines outlined in the Clinical Laboratory Standards Institute (CLSI) M38-A2. Isolates of 10 µL were extracted from each well, cultured on the SDA plates, and incubated for 4–7 days at 35 °C. The minimum concentration of the respective antifungal drug at which no colony was detected was identified as the Minimum Fungicidal Concentration (MFC). This test was performed in triplicate. The MIC index, defined as the ratio of the MFC to MIC (23,24), was calculated for each drug as shown in equation 1. Drugs were classified as fungicidal (MIC index≤ 2) or fungistatic (MIC index> 2) (25).

$$\text{MIC index} = \frac{\text{GM MFC}}{\text{GM MIC}} \quad \text{.....Eq. (1)}$$

Treatment outcomes

Upon suspicion of TI, an empirical therapy was initiated for all patients (n=45) to promptly address the fungal infection while awaiting the results of antifungal susceptibility testing. The empirical therapy consisted of the application of a topical gel containing 1% (w/w) terbinafine hydrochloride (HOE, Malaysia) to the affected areas. Additionally, a randomly selected subgroup of patients (n=23) was assigned to receive combination therapy, which involved the concurrent

use of the topical terbinafine gel along with oral griseofulvin (Royce Pharma, Malaysia). The griseofulvin dosage was 125 mg/day for children <13 kg, 250 mg/day for 13–24 kg, 500 mg/day for 24–35 kg, and 1000 mg/day for adults. The lesion area (LA) was measured using a transparent graph grid method. Lesion outlines were carefully traced onto a transparent sheet pre-calibrated with a 4 mm square grid. The total LA (cm^2) was then calculated by summing the number of fully covered grid squares and estimating partially covered squares. Measurements were performed at baseline and after one month of treatment to evaluate the efficacy of the therapeutic interventions in reducing the extent of affected LA. Additionally, patients were interviewed regarding their medication adherence, adverse events, and hygiene characteristics.

Statistical analysis

Categorical data were presented as frequency and percentage (%), while continuous data were presented as mean ± standard error measurement (SEM) where appropriate. Sociodemographic characteristics of diagnosed patients were analysed using the Chi-square test and Fisher's exact test to identify differences in frequencies between the two treatment groups. Antifungal susceptibility analysis and treatment outcome were analysed using the Analysis of variance (ANOVA) test with Duncan's post-hoc test. All statistical tests were conducted in IBM SPSS version 23 and the level of significance was set at $p<0.05$.

RESULTS

Prevalence of Tinea imbricata

Table I provides the epidemiological characteristics of TI within the studied population. A total of 45 individuals were diagnosed with TI, representing 7.91% of the total population of the five villages (n=569). Among the affected individuals, 23 were male and 22 were female, accounting for 7.52% and 8.37% of the population by gender, respectively. Analysis of age distribution revealed that children aged 15 years and below were the most affected age group in the whole population, representing 9.22%, followed by individuals aged 16–30 years (8.59%), 31–45 years (8.33%), 46–60 years (6.19%), and 61 years and above (6.02%). The highest prevalence was observed among individuals residing in Jeram Dedari, with 18.6% of the population affected. This prevalence was two times higher compared to those residing in Sungai Garam (8.33%), Sungai Sekin (7.29%), and Kampung Ulu Sat (9.6%). Additionally, the prevalence among individuals in Jeram Dedari was significantly ($p<0.05$) four times higher than among those residing in Becah Kelubi (4.57%).

Table I: The study population's demographic profile and TI diagnosis

Characteristics	Total		Diagnosed with Tinea imbricata		
	n (569)	% =100	n (45)	% 7.91	(45/569)
Gender					
Male	306	53.8	23	7.52	(23/306)
Female	263	46.2	22	8.37	(22/263)
Age					
<15	141	24.8	13	9.22	(13/141)
16-30	128	22.5	11	8.59	(11/128)
31-45	120	21.1	10	8.33	(10/120)
46-60	97	17.0	6	6.19	(6/97)
>61	83	14.6	5	6.02	(5/83)
Village					
Jeram Dedari	43	7.56	8	18.6	(8/43)
Sungai Sekin	96	16.9	7	7.29	(7/96)
Sungai Garam	108	19.0	9	8.33	(9/108)
Kampung Ulu Sat	125	22.0	12	9.6	(12/125)
Becah Kelubi	197	34.6	9	4.57	(9/197)

Clinical findings for Tinea imbricata diagnosis

Table II represents the distribution of affected body areas among patients with TI. The torso was found to be the most commonly affected region, with 80% of patients exhibiting lesions in this area. This was followed by the upper limb (75.6%), and the lower limb (64.4%). Conversely, patients displaying lesions on the face (11.1%), neck (11.1%), and ears (6.7%) regions were the least affected.

Table II: Distribution of affected body areas among patients with Tinea imbricata

Village	N	Body		Upper limb		Lower limb		Face		Neck		Ears	
Jeram Dedari	8	8	(100)	7	(87.5)	6	(75.0)	2	(25.0)	1	(12.5)	1	(12.5)
Sungai Sekin	7	5	(71.4)	3	(42.9)	4	(57.1)	0	(0)	1	(14.3)	0	(0)
Sungai Garam	9	8	(88.9)	7	(77.8)	4	(44.4)	3	(33.3)	0	-	1	(11.1)
Kampung Ulu Sat	12	9	(75.0)	10	(83.3)	9	(75.0)	0	(0)	2	(16.7)	1	(8.3)
Becah Kelubi	9	8	(88.9)	7	(77.8)	6	(66.7)	0	(0)	1	(11.1)	0	(0)
Total	45	36	(80.0)	34	(75.6)	29	(64.4)	5	(11.1)	5	(11.1)	3	(6.7)

Antifungal drug susceptibility testing

Table III revealed varying degrees of effectiveness on the commonly used antifungal agents against clinical isolate of *T. concentricum*. Terbinafine exhibited significant ($p<0.05$) potency (Geometric mean (GM) MIC=0.144 µg/ml) compared to griseofulvin (GM MIC=1.741 µg/ml), clotrimazole (GM MIC=5.897 µg/ml), and fluconazole (GM MIC=113.844 µg/ml). Additionally, terbinafine demonstrated fungicidal activity (MIC index = 1.375), as evidenced by the MIC index < 2. In contrast, griseofulvin (MIC index=2.747) and clotrimazole (MFC=128 µg/ml), exhibited fungistatic activity (MIC index >2). However, fluconazole exhibited neither fungicidal nor fungistatic activity at up to 128 µg/ml, indicating potential resistance against clinical isolate dermatophyte strains.

Table III: Antifungal susceptibility of clinical isolates of *Trichophyton concentricum* to commonly used antifungal agents in Malaysian healthcare settings

Antifungal drugs	MIC range	MIC_{50}/ MIC_{90}	Geometric Mean MIC	MFC range	Geometric Mean MFC	MIC index
Terbinafine	0.06–0.5	0.06/0.13	0.144[a]	0.06–1	0.198[a]	1.375
Griseofulvin	1–4	1/2	1.741[b]	2–16	4.782[b]	2.747
Clotrimazole	2–16	4/8	5.897[c]	4–32	22.291[c]	3.780
Fluconazole	32–128	64/128	113.844[e]	> 128	ud	-

"Values expressed in µg/ml except MIC index."

ud = undetermined.

[a-e] Mean values within a column with no common superscript indicate statistical significance at $p<0.05$ (ANOVA and Duncan's test).

Treatment modalities for Tinea imbricata

Following the classification of patients into two treatment modalities, the first group (n=22) received terbinafine gel alone, while the second group (n=23) underwent combination therapy involving terbinafine gel and oral griseofulvin for approximately 1 month (Table IV). Seven patients were excluded from the study due to them missing follow-up appointments or having relocated during subsequent visits. Comparative analysis between the two treatment groups revealed no significant differences ($p>0.05$) in most of the socio-demographic characteristics which suggest that initial patient profiles were well-balanced, minimizing potential confounding factors in treatment outcomes. Two significant differences ($p<0.05$) were identified between the two treatment groups. Firstly, there was an unequal distribution of villagers, with all patients residing in Kampung Ulu Sat (n=11) receiving terbinafine gel alone, while patients in Jeram Dedari (n=7) and Sungai Garam (n=7) received combination therapy of terbinafine gel and oral griseofulvin. The second significant difference ($p<0.05$) observed between the treatment groups was in bathing frequency. All villagers shared the same environmental conditions, including temperature and humidity, as they lived within the same rainforest area (26). Additionally, a majority of the patients in both treatment groups reported bathing more than three times daily. Despite the differences in treatment modalities, there was no significant disparity ($p>0.05$) in the average baseline of LA between the single therapy group (25.737 ± 17.0 cm2) and the combination therapy group (43.658 ± 28.1 cm2).

Table IV: Socio-demographic profile and baseline affected body areas of patients receiving terbinafine gel alone or combination therapy (terbinafine gel + oral griseofulvin)

Characteristics	Topical treatment [a] **n=19 (%)**	Combination treatment [b] **n=19 (%)**	*P* [c]	All (n=38)
Gender				
Male	7 (36.8)	12 (63.2)	0.105	19 (50.0)
Female	12 (63.2)	7 (36.8)		19 (50.0)
Age				
<15	7 (36.8)	4 (21.1)	0.692	11 (28.9)
16-30	4 (21.1)	5 (26.3)		9 (23.7)
31-45	4 (21.1)	5 (26.3)		9 (23.7)
46-60	3 (15.8)	2 (10.5)		5 (13.2)
>61	1 (5.26)	3 (15.8)		4 (10.5)
Village				
Jeram Dedari	0	7 (36.8)	<0.001	7 (18.4)
Sungai Sekin	4 (21.1)	1 (5.26)		5 (13.2)
Sungai Garam	1(5.26)	7 (36.8)		8 (21.1)
Kampung Ulu Sat	11 (57.9)	0		11 (28.9)
Becah Kelubi	3 (15.8)	4 (21.1)		7 (18.4)
Employment status				
Student	8 (42.1)	5 (26.3)	0.137	13 (34.2)
Worker	6 (31.6)	12 (63.2)		18 (47.4)
Housewife	5 (26.3)	2 (10.5)		7 (18.4)
Bathing frequency				
Once daily	7 (36.8)	1 (5.26)	0.026	8 (21.1)
Twice daily	2 (10.5)	7 (36.8)		9 (23.7)
≥ Three times daily	10 (52.6)	11 (57.9)		21 (55.3)
Bathe using soaps				
Yes	2 (10.5)	3 (15.8)	0.631	5 (13.2)
No	17 (89.5)	16 (42.1)		33 (86.8)
Frequency of changing clothes				
Once daily	6 (31.6)	2 (10.5)	0.253	8 (21.1)
Twice daily	5 (26.3)	8 (42.1)		13 (34.2)
≥ Three times daily	8 (42.1)	9 (47.4)		17 (44.7)
Habit of drying the body before wearing clothes				
Yes	16 (84.2)	15 (78.9)	0.676	31 (81.6)
No	3 (15.8)	4 (21.1)		7 (18.4)
Washing clothes with detergent				
Yes	1 (5.26)	0	0.311	1 (2.63)
No	18 (94.7)	19 (100.)		37 (97.4)
Family members having the same infection.				
Yes	11 (57.9)	9 (47.4)	0.516	20 (52.6)
No	8 (42.1)	10 (52.6)		18 (47.4)
Tinea imbricata disrupting daily life				
Yes	11 (57.9)	15 (78.9)	0.163	26 (68.4)
No	8 (42.1)	4 (21.1)		12 (31.6)
Missing taking the medication(s)				
Yes	4 (21.1)	4 (21.1)	0.654	8 (21.1)
No	15 (78.9)	15 (78.9)		30 (78.9)
Average baseline of affected lesion area (cm^2)	25.737±17.0	43.658±28.1	0.726 [d]	34.697±24.7

[a] Patients received 1% (w/w) terbinafine gel

[b] Patients received combination therapy of 1% (w/w) terbinafine gel and oral griseofulvin.

[c] Chi-squared test used unless stated otherwise

[d] Independent samples t-test used.

Impact of treatment modalities on Tinea imbricata lesions

Figure 2 reveals that patients treated with terbinafine gel demonstrated a significant ($p<0.001$) 8-fold reduction in the average affected LA($\bar{x}$ LA).Post-1-month treatment, the $\bar{x}$LA decreased to 3.684±1.522 cm2, with a range of 0–20 cm2, compared to pre-treatment, where the $\bar{x}$LA was 25.737±3.901 cm2, with a range of 8–72 cm2. Meanwhile, patients receiving a combination of terbinafine gel and oral griseofulvin experienced a highly significant ($p<0.001$) 276-times reduction in the $\bar{x}$LA. Following 1-month treatment, the $\bar{x}$LA reduced to 0.158±0.158 cm2, with a range of 0–3 cm2, compared to pre-treatment, where the $\bar{x}$ LA was 43.658±6.455 cm2, with a range of 12–100 cm2. Interestingly, there was a significant ($p<0.05$) 24-fold difference observed between the post-1-month treatment outcomes of patients receiving terbinafine gel alone and those receiving combination therapy of terbinafine gel and oral griseofulvin.

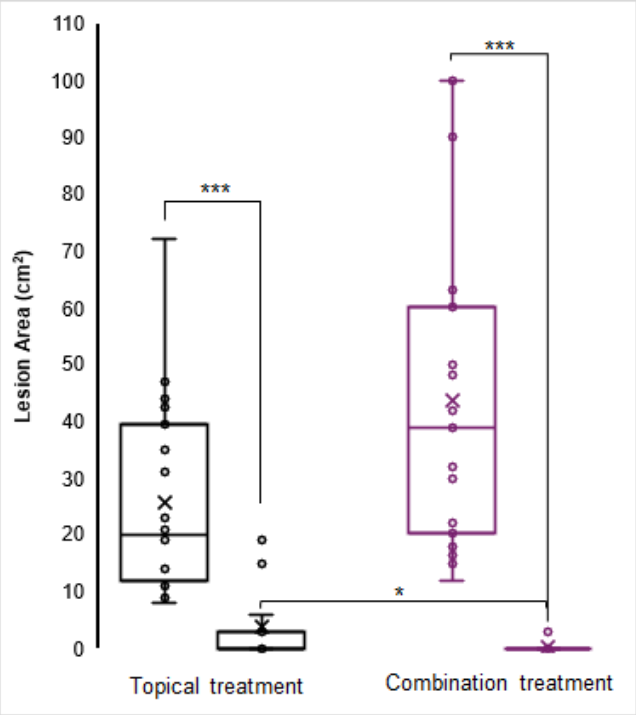

Figure 2: Impact of treatment modalities on Tinea imbricata lesions. Comparison of pre- and post-treatment reduction in lesion area with terbinafine gel alone and combination therapy (terbinafine gel + oral griseofulvin) (*p<0.05, ***p<0.001).

DISCUSSION

The findings of this study highlight the complex interplay between environmental, socio-economic, and cultural factors in influencing the prevalence and persistence of TI within the studied population. With an overall prevalence rate of 7.91%, slightly higher than the 7.5% prevalence reported by Er et al. (2024) among Negrito communities (8), it is evident that TI imposes a significant burden. Of particular concern is the disproportionate impact on children aged 15 years and below, who accounted for the highest prevalence rate of 9.22%. This observation has also been reported in other indigenous communities in the Solomon Islands (27), and West Kalimantan, Indonesia (28), which may reflect differences in exposure risk, humidity, poor hygiene, immune response, or behavioural factors among different age groups (4,29,30). The high prevalence of lesions on the torso, upper limb, and lower limb suggests that these areas are particularly susceptible to cutaneous mycosis due to factors such as the large areas of glabrous skin, which increase exposure and create favourable conditions for fungal growth (31).

Despite the implementation of national resettlement programs and the attraction of tourism, the communities in these villages continue to maintain semi-nomadic lifestyles. They engage in a rotational pattern of activities, alternating between tourism duties and traditional hunting and gathering practices in the forest. The designation of the national park as a protected area has indirectly safeguarded the Bateq community's indigenous rights, allowing them to continue their semi-nomadic way of life within the jungle environment. However, limited access to healthcare services due to geographic remoteness and low socioeconomic status could result in delayed diagnosis and treatment of TI, exacerbating the burden of the disease (18). Moreover, lower levels of education among community members contribute to limited knowledge about proper hygiene practices and preventative measures against fungal infections. Furthermore, our findings reveal concerning trends in hygiene practices among community members, with only 15.2% reported to be using soaps during bathing (n=5) and a mere 0.03% using detergents when washing clothes (n=1). These low rates of hygiene product usage highlight potential contributing factors to the prevalence of TI in the community (18). Given the popularity of international travel to these villages, physicians should be familiar with clinical manifestations of TI lesions for accurate diagnosis and timely intervention (31).

The global rise in antifungal-resistant superficial dermatophytes infections further complicates treatment. Resistance to conventional antifungal agents like terbinafine (14) and azole-based drugs (16), poses significant therapeutic challenges. Triazole antifungals, such as ketoconazole and itraconazole (32), have shown limited effectiveness, and fluconazole is consistently reported to have the lowest potency among this class (33). These trends highlight the pressing need for innovative solutions to address antifungal resistance effectively. A major challenge in interpreting antifungal susceptibility patterns for Trichophyton spp. lies in the absence of established clinical breakpoints within CLSI guidelines. Although epidemiological cutoff values (ECVs) have been proposed for rare molds, insufficient data exist to define ECVs for Trichophyton spp. Consequently, susceptibility assessments rely on comparative analyses of in-vitro potencies. To date, no antifungal

susceptibility tests have been conducted specifically on *T. concentricum* strains, making our study pioneering in this area. Our findings indicate significant ($p<0.05$) sensitivity of *T. concentricum* isolates to terbinafine (GM MIC=0.144 µg/ml; GM MFC=0.198 µg/ml), moderate effectiveness for griseofulvin (GM MIC=1.741 µg/ml; GM MFC=4.782 µg/ml) and clotrimazole (GM MIC=5.897 µg/ml; MFC=22.291 µg/ml), and a concerning lack of susceptibility to fluconazole, with no fungicidal or fungistatic activity even at high concentrations (128 µg/ml). These results align with existing literature on Trichophyton spp., where fluconazole MIC ≥64 µg/ml has been reported by Allahdadi et al. (2019) in Iran (34), Koehler et al. (2021) in southern Brazil (35), and Gill et al. (2023) in India (18), emphasizing a growing global trend of antifungal resistance and reinforcing terbinafine as the most effective treatment option for *T. concentricum* infections. Consequently, routine in-vitro susceptibility testing is essential for guiding effective clinical treatments and early identification of resistant strains.

Our study demonstrates significant reductions ($p<0.001$) in LA for both treatment groups, confirming the efficacy of terbinafine gel and combination therapy in managing TI. The substantial difference in reduction magnitude between the two treatment groups suggests that combination therapy offers superior efficacy ($p<0.05$) compared to topical therapy alone. This finding is consistent with previous studies indicating that combining topical and oral antifungals significantly reduces the duration required for complete clinical and mycological clearance of superficial fungal infections compared to topical treatment alone (36,37). The enhanced efficacy observed with combination therapy is likely due to the synergistic action of topical and systemic antifungals, promoting quicker and more complete lesion resolution. The observed differences in treatment outcomes also emphasize the importance of tailoring treatment regimens based on individual patient characteristics and disease severity. While topical terbinafine alone might be sufficient for managing mild to moderate cases of TI, combination therapy is recommended for severe or persistent cases (38). Additionally, environmental and behavioural factors, such as frequent bathing (55.4% of patients bathing more than three times daily) and frequent clothing changes (44.7% changing clothes more than three times daily), likely contributed to diminished efficacy of topical treatment by removing the medication from the skin surface. Hence, the use of combination therapy is advantageous in these situations. The high adherence rate among participants and absence of adverse effects further support the practicality and safety of both treatment approaches, reinforcing their clinical utility in managing TI.

To our knowledge, this represents the first investigation into the prevalence of TI, antifungal susceptibility and treatment modalities among the Bateq subtribe residing in the National Rainforest Park of Pahang, Malaysia. Nonetheless, several limitations warrant consideration. Firstly, the utilization of convenience sampling could limit the diversity of the study population and compromise the generalizability of the findings to other settings or populations. Secondly, socio-demographic characteristics, treatment adherence and occurrence of adverse effects were self-reported by participants, potentially introducing bias and affecting the accuracy of the data. Thirdly, the study's short follow-up period may limit the ability to assess long-term treatment outcomes and the risk of TI recurrence. Fourthly, although previous studies consistently identify *T. concentricum* as the causative organism of TI (4,27,39), and no co-infections were observed (8), future research should incorporate molecular analysis for accurate pathogen identification. Lastly, inadequate control group for comparison, which could limit the ability to draw definitive conclusions regarding the relative efficacy of different treatment modalities.

CONCLUSION

Our findings demonstrate the significant burden of TI among the Bateq subtribe (7.91% prevalence), particularly affecting children under 15 years. Antifungal susceptibility testing of clinical isolates of *Trichophyton concentricum* showed high sensitivity to terbinafine and griseofulvin, while resistance to fluconazole was observed, with no fungicidal activity detected up to 128 µg/ml. Combination therapy with terbinafine gel and oral griseofulvin demonstrated superior efficacy compared to terbinafine gel alone in reducing x1LA. Further research is warranted to investigate long-term treatment outcomes and genetic factors influencing susceptibility.

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