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ABSTRACT

Introduction: Tinea unguium is a common nail infection. We conducted a retrospective ten-year study of the patient demographics and species distribution of dermatophytes causing tinea unguium in a tertiary hospital from Singapore.

Methods: Results of fungal nail cultures were retrieved from our hospital’s microbiology department. Samples from nail scrapings and clippings were inoculated onto agar plates (Sabouraud dextrose agar with chloramphenicol and Mycosel agar). Nail specimens that grew dermatophytes were included in the study.

Results: Overall, 229 (men: n = 164, 71.6%; women: n = 65, 28.4%) nail specimens grew dermatophytes. Mean patient age was 58 (range 18–93) years. A majority of specimens came from patients aged over 50 years (n = 162, 70.7%) and 60–79 years (n = 100, 43.7%). Ethnically, 160 (69.9%) patients were Chinese, 36 (15.7%) Indian, 18 (7.9%) Malay and 15 (6.6%) of other ethnicities. Among dermatophytes isolated were Trichophyton rubrum (n = 93, 40.6%), Trichophyton mentagrophytes (n = 60, 26.2%), unidentified Trichophyton spp. (n = 57, 24.9%), Trichophyton tonsurans (n = 10, 4.4%), Epidermophyton floccosum (n = 5, 2.2%), Trichophyton verrucosum (n = 2, 0.9%), Trichophyton soudanense (n = 1, 0.4%) and Trichophyton violaceum (n = 1, 0.4%).

Conclusion: A majority of isolates were from elderly patients. Compared to Singapore’s general population, patients of Indian and other ethnicities were over-represented for tinea unguium when compared to Chinese and Malay patients. Trichophyton rubrum was the most common dermatophyte isolated while Trichophyton verrucosum, Trichophyton violaceum and Trichophyton soudanense were rare causes of tinea unguium.

Keywords: fungus, nail, onychomycosis, tinea unguium
INTRODUCTION

Nail conditions are a common complaint in general medical practice and dermatology consultations. Many patients see their family doctor or are referred to the dermatologist because they suspect their nail problem to be a fungal infection. A literature review by Ramesh et al concluded that onychomycosis, also known as tinea unguium, is a common fungal infection that constitutes 15% of all nail disturbances, while fungal infection of the nails constitutes 10% of all patients with dermatophytosis.\(^{(1)}\) In 2012, Hay and Baran estimated that only 18%–40% of all nail disorders were onychomycoses, and 30% of all dermatomycoses were nail infections.\(^{(2-4)}\) Even psoriasis of the nails can produce subungual hyperkeratosis, onycholysis and total nail dystrophy,\(^{(2)}\) which may mimic tinea unguium. Hence, as not all nail conditions are caused by fungal infection, it is important to confirm the diagnosis of onychomycosis before starting treatment.

English proposed that ‘tinea unguium’ should be confined to nail infections caused by dermatophytes while ‘onychomycosis’ should include nail infections attributable to any fungus that may be dermatophyte, mould or yeast.\(^{(5)}\) Fungi cause onychomycosis by invading the nail plate or nail fold. There are a limited number of fungi capable of invading healthy nail keratin; these include some dermatophytes that possess keratinases, which allow them to use keratin as a substrate. Dermatophytes usually invade healthy nails. They may also invade dystrophic nails, which are especially common in elderly patients.\(^{(6)}\)

The gold standard for diagnosing tinea unguium is to take a sample from the diseased nail and send it to a laboratory for culture test, and microscopic examination. As the appearance of mycelium under microscope alone may not indicate a dermatophyte as the causative agent, a final diagnosis can be established only after culture results become available.\(^{(6)}\) Any dermatophyte that is cultured from the nail is considered a pathogen and requires treatment.
In Singapore, Lim et al conducted a prospective study in 1992 on dermatophyte- and non-dermatophyte onychomycoses at the Singapore National Skin Centre,\(^7\) which provides outpatient care. The present retrospective study on patients with tinea unguium at the Singapore General Hospital (SGH) is the first to come close to that of Lim et al by studying similar patients in a hospital setting. The objective of our study was to determine the demographics and species distribution of dermatophytes among patients with tinea unguium in a tertiary hospital from a multiracial country in Asia.

**METHODS**

We conducted a retrospective study of patients with tinea unguium at SGH over a ten-year period between 1 January 2005 and 31 December 2014. SGH is a tertiary hospital situated within the SingHealth complex, which also houses the National Cancer Centre Singapore, National Heart Centre Singapore, National Dental Centre Singapore, Singapore National Eye Centre, Outram Polyclinic (SingHealth) and Duke-NUS Medical School.

Culture results of nail specimens collected during the study period were retrieved from the Department of Microbiology, SGH. The results of all dermatophyte nail infections were analysed. The source of specimen was not stated as a fingernail or toenail in most of the requests, nor was it possible to differentiate between the two during our analysis. As the data for this retrospective study were retrieved from the microbiology department, the clinical features of tinea unguium infections were not available.

Besides patient demographics, the species distribution of dermatophytes that caused tinea unguium in our patients was studied. Mycological cultures were used to confirm onychomycosis caused by dermatophytes.

 Scrapings or cuttings from nails and nail beds were collected in sterile bottles and sent to the laboratory. The scrapings were picked up using sterile sticks and inoculated onto the
agar plate. If the piece was too large, the nail would be cut into smaller pieces before being inoculated onto the agar plate, Sabouraud dextrose agar with chloramphenicol, and Mycosel agar that contained cycloheximide and chloramphenicol. The agar plates were then incubated at 30°C. The culture plates were examined once a week and discarded after four weeks if there was no growth. Any fungi that grew would be planted onto potato dextrose agar for gross and microscopic examinations. If necessary, urea hydrolysis was done. Trichophyton agar nos. 1 and 4 were used to identify the *Trichophyton* spp., the usefulness of which was limited to certain types of *Trichophyton* spp. only.

There are not many biochemical (phenotypic) tests that can differentiate *Trichophyton* spp. to the species level. *Trichophyton* was diagnosed mainly based on the gross morphology of the mould colonies (e.g. size, colour, texture and rate of growth) and their microscopic features. *Trichophyton* have macroconidia and microconidia arranged along the hyphae, which are used to identify the *Trichophyton* spp. Some *Trichophyton* spp. had poor sporulation on potato dextrose agar. When the macroconidia were lacking or not well formed and the microconidia were few despite being incubated for up to three weeks, the species name could not be identified and specimen would be reported as unidentified *Trichophyton* spp. *Trichophyton mentagrophytes* was not subspeciated further, as it was difficult to subspeciate based on data from only the microscopic examination and phenotypic tests. These were the resources used for mould identification. Molecular sequencing would have been needed to subspeciate, but this was not routinely done for our nail specimens. At our centre, molecular sequencing is only done for deep-site specimens from fluids and blood culture, or when it is needed to guide management.

Data was retrieved as counts and percentages for the distributions of dermatophytes isolated, gender and ethnicity. Age distribution was depicted graphically via a histogram. A one-sample chi-square test was used to compare the differences between the ethnic make-up
of our patients and the general Singapore population. A p-value < 0.05 was considered to be statistically significant.

RESULTS

There were 229 specimens that grew dermatophytes. Of these, 128 (55.9%) specimens were from the dermatology outpatient clinic, 98 (42.8%) specimens were from inpatients seen at the hospital’s Department of Dermatology and 3 (1.3%) specimens were from the day surgery centre. There were 164 (71.6%) specimens isolated from men and 65 (28.4%) specimens from women (male:female ratio = 2.5:1) (Table I).

Table I. Characteristics of patients (n = 229).

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>164 (71.6)</td>
</tr>
<tr>
<td>Female</td>
<td>65 (28.4)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
</tr>
<tr>
<td>Chinese</td>
<td>160 (69.9)</td>
</tr>
<tr>
<td>Malay</td>
<td>19 (8.3)</td>
</tr>
<tr>
<td>Indian</td>
<td>36 (15.7)</td>
</tr>
<tr>
<td>Others</td>
<td>14 (6.1)</td>
</tr>
</tbody>
</table>

The mean age of patients was 58 (range 18–93) years. Although there is a neonatal department at SGH, the tertiary hospital largely serves adult patients. Culture results were from patients of different age groups, with patients aged 50–59 years, 60–69 years and 70–79 years contributing the majority of specimens (n = 137, 59.8%). Overall, patients aged over 50 years contributed 162 (70.7%) specimens (Table II and Fig. 1).

Table II. Patient distribution by age.

<table>
<thead>
<tr>
<th>Age group (yr)</th>
<th>No.</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
<td>Male+Female</td>
</tr>
<tr>
<td>10–19</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>20–29</td>
<td>6</td>
<td>6</td>
<td>12</td>
</tr>
<tr>
<td>30–39</td>
<td>14</td>
<td>7</td>
<td>21</td>
</tr>
</tbody>
</table>
Ethnically, 160 (69.9%) specimens were isolated from Chinese patients, 36 (15.7%) from Indian patients, 18 (7.9%) from Malay patients and 15 (6.6%) from patients of other ethnicities. The ethnic make-up of our patients with tinea unguium caused by dermatophytes was different from that of the general Singapore population, which is 75.3% Chinese, 13.8% Malay, 8.6% Indian and 2.3% other ethnicities.\(^{(8)}\) In our cohort, patients of Indian and other ethnicities were over-represented while Chinese and Malay patients were under-represented (p = 0.001) (Table I).

Among the dermatophytes isolated were *Trichophyton rubrum* (n = 93, 40.6%), *Trichophyton mentagrophytes* (n = 60, 26.2%), unidentified *Trichophyton* spp. (n = 57, 24.9%), *Trichophyton tonsurans* (n = 10, 4.4%), *Epidermophyton floccosum* (n = 5, 2.2%), *Trichophyton verrucosum* (n = 2, 0.9%), *Trichophyton soudanense* (n = 1, 0.4%) and *Trichophyton violaceum* (n = 1, 0.4%) (Table III).

**Table III. Dermatophytes isolated from nail specimen cultures (n = 229).**

<table>
<thead>
<tr>
<th>Dermatophyte</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Trichophyton rubrum</em></td>
<td>93 (40.6)</td>
</tr>
<tr>
<td><em>Trichophyton mentagrophytes</em></td>
<td>60 (26.2)</td>
</tr>
<tr>
<td>Unidentified <em>Trichophyton</em> spp.</td>
<td>57 (24.8)</td>
</tr>
<tr>
<td><em>Trichophyton tonsurans</em></td>
<td>10 (4.4)</td>
</tr>
<tr>
<td><em>Epidermophyton floccosum</em></td>
<td>5 (2.2)</td>
</tr>
<tr>
<td><em>Trichophyton verrucosum</em></td>
<td>2 (0.9)</td>
</tr>
<tr>
<td><em>Trichophyton violaceum</em></td>
<td>1 (0.4)</td>
</tr>
<tr>
<td><em>Trichophyton soudanense</em></td>
<td>1 (0.4)</td>
</tr>
</tbody>
</table>
DISCUSSION

Tinea unguium affects not only the cosmetic appearance of nails but also the patient’s dexterity. It serves as a portal of entry for bacterial infection into the patient’s skin and may even aid in spreading the dermatophyte infection to the skin and nails of other people in the community.

Nail clippings from the distal end of the nails are the usual specimens sent for culture for establishing a diagnosis of onychomycosis before starting treatment. However, dermatophytes are often dead by the time they reach the distal end of the nail. This may possibly be because the dermatophyte is unable to survive in keratin, which is chemically much harder than the inner and middle nail plates that are its preferred habitat, or possibly due to loss of nutrients or moisture.\(^{(5)}\) Given this difficulty in successfully culturing dermatophytes from nail specimens, the likelihood of false-negative cultures remains high even for patients with nail infections. Diagnosing tinea unguium based primarily on laboratory cultures may thus suggest false low prevalence that understates its actual magnitude in the general population.

Various methods have been adopted to overcome the difficulty in isolating fungi from nail clippings. One method is to use a dental drill fitted with a suction nozzle, as proposed by English.\(^{(5)}\) This instrument has raised the success rate of culture from microscopically positive nails from the usual rate of 50% to nearly 88%.\(^{(5)}\) However, the instrument is not practical for routine laboratory use.

To the best of our knowledge, there has been no study on the prevalence of tinea unguium in Singapore. In a prospective study done in the general adult population in Madrid, Spain, in 2000 the prevalence of tinea unguium was 2.8% (men: 4.0%; women: 1.7%).\(^{(9)}\) This prevalence parallels that of psoriasis,\(^{(10)}\) which poses a significant health problem as well.
In our retrospective study of patients with tinea unguium over ten years, we found that most patients for whom dermatophytes were isolated were elderly – 48.9% (n = 112) of dermatophyte specimens were from patients aged 60 years and above, and there were 37 (16.2%) patients aged 80–89 years and 25 (10.9%) patients aged 90–99 years. There are several reasons for tinea unguium being more common among elderly people. Young children seldom develop tinea unguium because their nails grow faster than adults’ nails, and this faster growth rate reduces the chances of dermatophytes invading their nail plates.\(^6\) As people age, their nails grow at a slower rate, and thus the likelihood of their nail plates being invaded by dermatophytes become higher. The nails of elderly people may also be subject to minor trauma due to poor eyesight, impaired mobility and poor nail care. Such dystrophic nails may be prone to invasion by dermatophytes, and even onycholysis and onychogryphosis.\(^6\) Other factors that predispose patients to tinea unguium include peripheral vascular diseases and diabetes mellitus, both of which are common comorbidities among elderly people.

In our study, men were affected more by tinea unguium than women (male:female ratio was 2.5:1). Our finding was similar to a study by Perea et al who found the male:female ratio among patients with tinea unguium in Spain to be 2.4:1.\(^9\) Men have tinea unguium more commonly than women as they tend to wear closed footwear and because their work and lifestyles may be predisposing factors.

Singapore is a multiracial country, with people of Chinese (majority), Malay, Indian and other ethnicities. In the ethnic make-up of its general population, people of Indian and other ethnicities form a small proportion when compared to Chinese and Malay people. However, in our study, significantly higher proportions of patients of Indian and other ethnicities had tinea unguium when compared to Chinese and Malay patients. This was in
contrast to a 1983 study by Ramesh et al where the incidence of toenail infection in India was found to be extremely low because the majority of people were barefoot.\(^{(1,11)}\)

According to English, the most common dermatophytes that cause tinea unguium in Europe and North America were *Trichophyton interdigitale* (*T. mentagrophytes* var *interdigitale*) and *T. rubrum*.\(^{(5)}\) Similarly, Zaias also summarised in a review that the dermatophytes causing tinea unguium worldwide were *T. rubrum* and *T. mentagrophytes* in Europe and America.\(^{(12)}\) Hay listed *E. floccosum*, *T. rubrum* and *T. interdigitale* as the most common dermatophytes causing tinea unguium.\(^{(6)}\) In Hong Kong, Kam et al surveyed patients attending the Government Dermatology Clinics over an eight-year period from 1 January 1987 to 31 December 1994, and reported that, among 152 single infections with dermatophytes and yeasts, the most common dermatophytes were *T. rubrum* (n = 68, 44.7%), *Trichophyton* spp. (n = 17, 11.2%) and *T. mentagrophytes* (n = 6, 3.9%).\(^{(13)}\)

SGH is a tertiary hospital with over 30 clinical departments that treats patients with multiple comorbidities, including solid organ transplant recipients, haematological patients and oncology patients who are immunocompromised and more prone to infection, including fungal infection of the skin and skin appendages. Infections in immunocompromised patients may be caused by unusual pathogens, have atypical presentation, and run a protracted course with increased morbidity and mortality. In our study, the most common dermatophytes were *T. rubrum* (40.6%), *T. mentagrophytes* (26.2%) and unidentified *Trichophyton* spp. (24.9%). Similar to Kam et al from Hong Kong,\(^{(13)}\) we too found that *T. rubrum* was the most common cause of tinea unguium in Singapore and *T. mentagrophytes* was a common cause of tinea unguium in Asia. Overall, *T. rubrum* was the most common dermatophyte that caused tinea unguium worldwide.\(^{(1)}\) *T. rubrum* is an anthropophilic fungus that has become the most widely distributed dermatophyte in humans. It frequently causes chronic infections of the skin and nails.\(^{(14)}\)
T. mentagrophytes was the second most common cause of tinea unguium in our study. We did not subspeciate T. mentagrophytes, however, as it is difficult to do so based merely on microscopic examination and phenotypic tests. For this reason, we were unable to establish how many of these specimen were T. interdigitale.

In the study by Hay, E. floccosum was one of the commonest dermatophytes causing tinea unguium. However, in our study, only 5 (2.2%) specimens grew E. floccosum. Likewise, Kam et al also found that, among 152 single infections with dermatophytes and yeasts in Hong Kong, only 1 (0.7%) specimen grew E. floccosum.

There were a few uncommon species that caused tinea unguium in our study. T. tonsurans is a common cause of tinea capitis among Australian Aborigines and African Americans. Although T. tonsurans can cause nail infection, it was not isolated in the study by Hay. In our study, T. tonsurans was isolated from 10 (4.4%) patients.

T. soudanense is an anthropophilic fungus that frequently causes tinea capitis in Africa. It is rarely reported as a cause of tinea unguium. The presence of T. soudanense was not reported by Hay. However, we had one patient with tinea unguium caused by T. soudanense. It is unlikely that this diagnosis was due to misidentification, as T. soudanense presents with a typical reflexive branching not seen in any other Trichophyton spp. on microscopic examination.

The natural habitat of T. verrucosum is cattle and it causes ringworm infection in these animals. It rarely causes infection among humans, and when present, such infection is the result of close contact with cattle or infected fomites, causing very inflammatory tinea capitis, tinea barbae or tinea corporis. T. verrucosum has rarely been reported to cause nail infection. However, we reported two patients with tinea unguium caused by T. verrucosum. One of these patients was a renal transplant patient whose immunocompromised status may have predisposed her to the infection.
There were some limitations to our retrospective study. There were 57 specimens that grew *Trichophyton* spp. that were not further identified. Likewise, *T. mentagrophytes* was also not further subspecialised. Another limitation was that the cultured specimens were not categorised as finger or toenail infection, and there was no correlation between the different dermatophytes and the various clinical features of tinea unguium.

In conclusion, our retrospective study at SGH over a ten-year period showed that 48.9% of patients with tinea unguium were aged 60 years and above. With increasingly ageing population worldwide, tinea unguium should be expected to become an emerging health problem, as older people are more prone to the infection. We reported a higher proportion of patients of Indian and other ethnicities with tinea unguium in our cohort. *T. rubrum* was the most common dermatophyte isolated while *T. verrucosum, T. violaceum* and *T. soudanense* were rare causes of tinea unguium in our study.

**ACKNOWLEDGEMENT**

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**FIGURE**

![Age distribution of patients by gender.](image)

**Fig. 1** Age distribution of patients by gender.