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Clinico-mycological study of onychomycosis in Botswana

Abstract

Background: Onychomycosis is a fungal disease of the toenails or fingernails that may include any part of the nail unit, including the matrix, bed, or plate. The causative organisms of onychomycosis are dermatophytes, Candida (yeasts), and non-dermatophytic molds, associated with different clinical presentations.

Methods: A retrospective study was carried out including the patients diagnosed with onychomycosis at the National Health Laboratory, Gaborone (Botswana), from January 2009 to December 2009. The objective of the study was to find out the predominant species and most common clinical form of onychomycosis in Botswana.

Results: 59 patients were diagnosed with onychomycosis (37 females and 22 males). *Trichophyton violaceum* (*T. violaceum*) was found to be the predominant species (44 patients, 74.58%) with male to female ratio of 10:34 and the commonest clinical type was endonyx onychomycosis (45 patients, 76.27%), followed by distal subungual onychomycosis (6 patients, 10.17%), white superficial onychomycosis (4 patients, 6.78%) and 4 (6.78%) cases of candida paronychia. Fingernail involvement was more common (48 patients, 81.35%) compared to toenail involvement (11 patients, 18.64%, all males).

Conclusion: Efforts ought to be made for the precise diagnosis and timely treatment of onychomycosis as it does not ordinarily cure by itself and can trigger more infectious lesions in other parts of the body. The treatment of onychomycosis is aimed at the eradication of the causative organism (both clinical and mycological cure). HIV status should be investigated where multiple fingernails or toenails are involved.

Keywords: *Trichophyton violaceum*, *Trichophyton interdigitale*, *Trichophyton tonsurans*

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Introduction

The term 'Onychomycosis' includes tinea unguium and also infection by non-dermatophyte fungi including yeasts. In 80-90% cases, the fundamental causative pathogens are *Trichophyton rubrum* and *Trichophyton interdigitale*.[1–4] About 2-11% cases of onychomycosis are due to non-dermatophyte fungi such as *Acremonium spp*., *Alternaria spp*., *Aspergillus spp*., *Fusarium spp*., *Scytalidium spp*. and *Scopulariopsis spp*. About 2-10% fungal nail infections are due to yeasts, including *Candida spp*.[5–9] These infections are frequently under diagnosed because of poor healthcare services in underdeveloped countries. A nail has the function of protecting the distal phalanx and the surrounding tissues from the trauma.[10] The prevalence of onychomycosis increases with immunosuppression (HIV/AIDS, diabetes, use of immunosuppressive therapies, cancer chemotherapy or antibiotics), increasing age, repeated injuries on nail, poor hygiene of nails and foot including occlusive foot wears, poor peripheral circulation, repeated exposure to pathogenic fungi and increasing use of health clubs for sports, swimming pools.[11]

Also, the prevalence of onychomycosis is increasing in Western countries, probably due to lifestyle changes and ageing of the population. About 10% of the general population, 20% of the population aged >60years, up to 50% of people aged >70years and up to one-third of diabetic individuals have onychomycosis.[12] Onychomycosis may have a genetic predisposition, but only in a very less percentage of persons.[13] The condition of nails represents the social status as observed by Gonzalez-Serva, 1990.[14] Onychomycosis constitutes 50% of the nail problems.[15]

There are five major clinical presentations of onychomycosis

i. Distal and lateral subungual onychomycosis (DLSO)
ii. Proximal subungual onychomycosis (PSO)
iii. Superficial white onychomycosis (SWO)
iv. Endonyx onychomycosis (EO)
v. Total dystrophic onychomycosis (TDO)

Methods

A retrospective study was carried out including the patients diagnosed with onychomycosis at the National Health Laboratory, Gaborone (Botswana), from January 2009 to December 2009. A total of 165 patients either clinically diagnosed or suspicious of onychomycosis were sent to the mycology laboratory for the collection of the samples. To avoid misdiagnosis as nail psoriasis, lichen planus, contact dermatitis, nail bed tumors such as melanoma, trauma, or yellow nail syndrome, laboratory confirmation was performed. The nails were cleaned with 70% isopropyl alcohol and samples were taken. Sterile nail clippers and No. 15 surgical blades were used to collect nail clippings and subungual debris in sterile petri dishes and labeled. Potassium hydroxide (20% KOH) mounts were prepared to look for the fungal elements.

Samples were inoculated on two plates of Sabouraud's dextrose agar with chloramphenicol and Derm agar. One plate was incubated at 37°C and one at 25°C along with the Derm agar plate. Candida species were differentiated on Chromogenic candida agar. For dermatophytes, KOH and/or culture positive samples were considered positive. For non-dermatophyte molds, both KOH and culture positive samples were considered positive. Also, a second sample was taken and if both KOH and culture were positive, it was considered positive. Patients with only positive direct microscopy and negative culture were excluded. The criteria for the diagnosis of onychomycosis caused by non-dermatophyte molds were based on

a. Fungal elements seen in KOH preparation on microscopy

b. Growth of the same mold in all duplicate culture

c. No growth of a dermatophyte or yeast in all the cultures

When the filaments were seen on the light microscopy but showed a non-dermatophyte growth on culture, then another nail specimen was examined by light microscopy and culture to confirm non-dermatophyte mold. Lacto phenol Cotton blue (LPCB) mounts were prepared in order to study the microscopic structures in details (Figure 4). The standard basic tests such as urease and in vitro hair perforation test were performed for the differentiation of *T. interdigitale* and *T. rubrum*.

Results

A total of 59 patients were found positive following the criteria and diagnosed with onychomycosis. The most common clinical pattern was endonyx onychomycosis (EO) i.e., 45 patients (76.27%) (Figure 5), followed by distal subungual onychomycosis (DSO) 6 patients (10.17%), total dystrophic onychomycosis (TDO) 5 patients, white superficial onychomycosis (WSO) 4 patients (6.78%) and 4 patients (6.78%) of candida paronychia (Table 1). We did not found proximal subungual onychomycosis in any of our patients. All the six cases of total dystrophic onychomycosis (TDO) were KOH and culture negative and were not included. These patients were females in the age group of 20-40years.

Table 1 Clinical pattern of onychomycosis

S. No.	Clinical types	Number & percentage
1	Distal Subungual Onychomycosis (DSO)	6 (10.17%)
2	White Superficial Onychomycosis (WSO)	4 (6.78%)
3	Proximal Subungual Onychomycosis (PSO)	0 (0)
4	Endonyx Onychomycosis (EO)	45 (76.27%)
5	Total Dystrophic Onychomycosis (TDO)	5 - Not included
6	Candida paronychia	4 (6.78%)
	Total	59 (100%)

Figure 1 *Trichophyton interdigitale*.

Table 2 Distribution of onychomycosis pathogens by age groups and fingernails/toenails involvement

Age group (in years)	*T. violaceum*		*T. interdigitale*		*T. tonsurans*		Non-dermatophytic molds		*Candida albicans*	
	Fingernails	Toe-nails	Finger-nails	Toenails	Finger-nails	Toenails	Finger-nails	Toenails	Fingernails	Toenails
0-15	04 (6.77%)	-	-	01 (1.69%)	-	-	-	-	01 (1.69%)	-
16-30	11 (18.64%)	-	-	01 (1.69%)	-	01 (1.69%)	-	01 (1.69%)	02 (3.38%)	-
31-45	10 (16.94%)	-	-	01 (1.69%)	-	-	-	02 (3.38%)	-	-
46-60	07 (11.86%)	-	-	-	-	-	-	01 (1.69%)	-	-
>61	12 (20.33%)	-	-	-	-	-	-	02 (3.38%)	01 (1.69%)	01 (1.69%)

Table 3 Onychomycosis pathogens

Species	Number of isolates	Male: Female	Percentage
T. violaceum	44	10:34	74.58
T. interdigitale	3	3:00	5.09
T. tonsurans	1	1:00	1.69
Aspergillus sp.	3	3:00	5.09
Fusarium sp.	2	2:00	3.39
Alternaria sp.	1	1:00	1.69
Candida albicans	4	0:04	6.78
Candida parpsilosis	1	1:00	1.69
Total	59	21:38	100

Out of total 59 patients with onychomycosis, 37 patients (62.7%) were females and 22 patients (37.2%) were males (Table 2). Fingernail involvement was more common (48 patients, 81.3%) compared to toenail involvement (11 patients, 18.64%, all males). In the age group of 0-15years, we found four cases of tinea unguium of fingernails due to *T. violaceum* (Figures 2,4,6,7,8) and one case of toenail involvement due to *T. interdigitale* (Figure 1). In three HIV positive females, fingernails were bilaterally involved with culture positive for *T. violaceum* (Figure 9). 34 (57.62%) females and 10 (16.94%) males had onychomycosis of the fingernails due to *T. violaceum* (Table 3). Out of four male patients, onychomycosis of toenails due to *T. interdigitale* was found in 3 patients (5%) (Table 3) and *T. tonsurans* (Figure 3) was insolated in 1 patient (1.69%). Non-dermatophyte molds were isolated from the toenails of 6 (10%) male patients and candida from 1 (1.69%) male patient. Onychomycosis of the fingernails due to candida was isolated in 3 (5.08%) females and of toenail in 2 (3.38%) male patients (Table 2). HIV status was known in 15 patients only. One HIV positive female patient was on azidothymidine and had melanonychia along with tinea unguium of fingernails due to T. violaceum (Figure 10). Distribution of tinea unguium of the fingernails due to *T. violaceum* as shown in Figure 11, shows the highest prevalence among the age group 16-30 years and second highest among 31-45years age group. These possibly correspond to the highest prevalence of HIV/AIDS among these age groups.

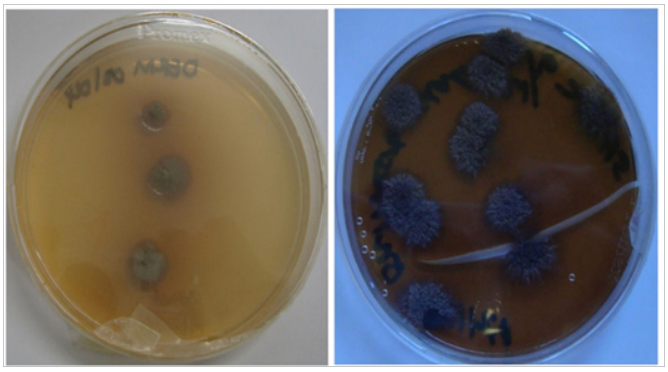

Figure 2 (a) Colonies of *T. violaceum* with waxy surface. (b) Verrucose colonies of *T. violaceum* with deep violet pigment.

Figure 3 *Trichophyton tonsurans.*

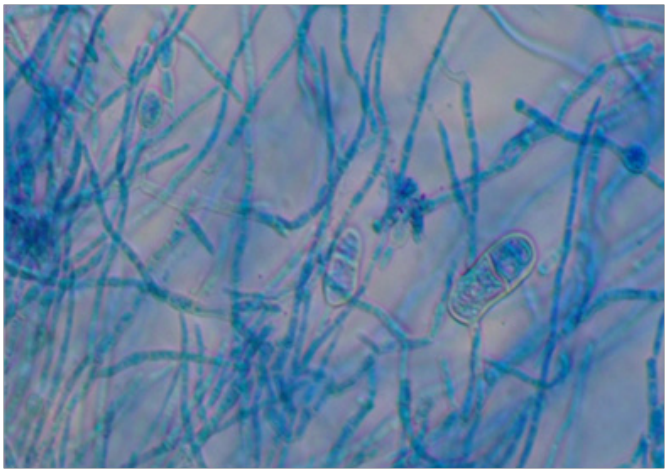

Figure 4 *Trichophyton violaceum* (Lacto Phenol Cotton Blue mount). Irregularly branched hyphae with intercalary chlamydoconidia and clavate two-celled macroconidia. Magnification X400.

Figure 5 Endonyx onychomycosis in a HIV positive male.

Figure 6 Tinea unguium. *T. violaceum* was isolated.

Figure 7 A 10-years old boy with tinea unguium (endonyx type) of left hand affecting nails of middle, ring and little fingers.

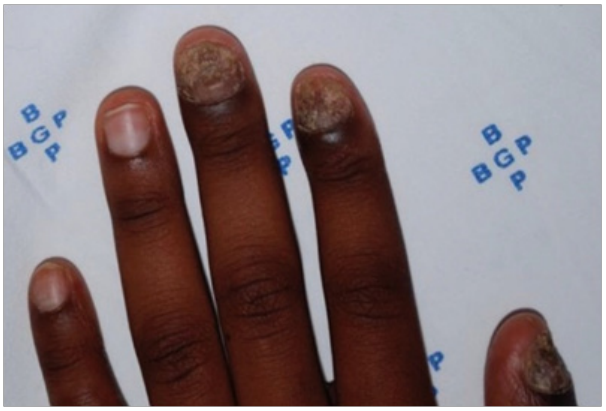

Figure 8 Tinea unguium of the left hand in a 14-years old male, affecting nails of thumb, index and middle fingers.

Figure 9 Tinea unguium (endonyx type) of all the nails in a HIV positive 22years old female.

Figure 10 Tinea unguium of all the fingernails with melanonychia in a HIV positive 51years old female. She was on azidothymidine.

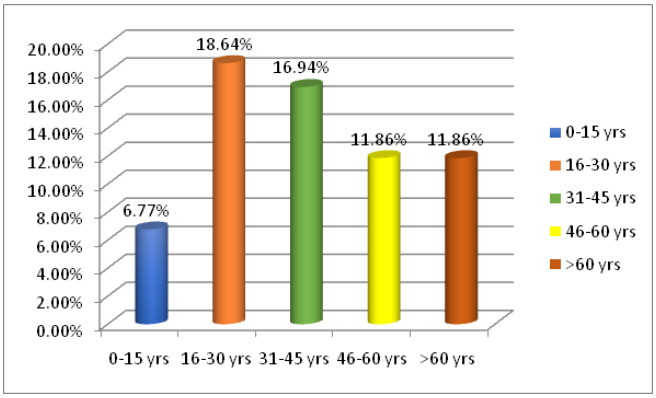

Figure 11 Bar diagram of onychomycosis due to *T. violaceum* among different age groups.

Discussion

Onychomycosis is caused by dermatophytes, non-dermatophyte molds (NDMs), and yeasts. Dermatophytes are the main causative agent in temperate climates, whereas Candida and non-dermatophyte molds in tropical regions.[16] It is traditionally a disease of the elderly.[17] It has a significant impact on patient's life and may cause psychological, social or employment related problems.[18]

Overall, dermatophytes are most commonly implicated, accounting for 90% of toenail infections and 50% of fingernail infections, and *T. rubrum* is responsible for most cases worldwide.[19] But scenario here in Botswana differs to a great extent from other geographical locations. In our study, we found *T. violaceum* as the predominant species accounting for 100% fingernail infections.

Onychomycosis is one of the early manifestations of HIV infection with a prevalence of 15-40%.[20] It is four times more common in HIV infected individuals than in the general population, which is reported to be up to 23% when their *T-lymphocytes* count is as low as 400/mm^3 (normal range: 1200-1400/mm^3), usually affecting all finger-nails and toe-nails.[21–23] Multiple nail involvement, isolation of both common and rare species, and resistance to treatment are the characteristics of onychomycosis in HIV.[20] Proximal subungual onychomycosis is usually an indication of HIV infection.[24–26] Botswana has the second-highest HIV infection rate in the world after Swaziland, with one in three adults infected. Females were infected more than males (21 males, 38 females), this can be related to the high prevalence of HIV

in females (28.9%) as compared to males (18.9%) during the period 2007-2009.[27] Population migration during the world wars led to the distribution of *T. rubrum* from its source regions to the new places like Europe and America.[28,29]

The first documented case of onychomycosis in US has been reported in 1928.[28,30] The prevalence of tinea pedis and onychomycosis increased in 20th century during the World War II and the Korean and Vietnam wars and due to the occlusive footwear and population migration. Vietnam war resulted in increased prevalence of *T. rubrum* worldwide.[31] But in Botswana, 74.58% cases of onychomycosis are due to *T. violaceum*. The authors did not report a single case due to *T. rubrum*. The involvement of the fingernails is the most common. The Asian Achilles Survey conducted in the late 1990s confirmed that the prevalence of onychomycosis is relatively low in Asian countries.[32]

Onychomycosis in children was thought to be more frequent in fingernails due to *Candida spp*.[33] But we found *T. violaceum* 4 (6.77%) to be the predominant species for fingernail infection in children (up to 15 years of age) as well. The reason for low frequency of onychomycosis in children is due to faster nail growth, lower incidence of tinea pedis and less exposure to spores, less chances of nail injuries and smaller surface area. Patients with Down's syndrome have more chances of onychomycosis as studied in Mexico.[34] High prevalence of onychomycosis in children could be either due to high prevalence of tinea capitis[27] and/or HIV. Other reasons include fungal infections in the other family members, pre-existing tinea pedis, physical activities, trisomy 21, obesity and diabetes mellitus.[35] In a study held at Colorado, 46.8% children suffered from onychomycosis, with high prevalence at the age group between 6-10.[36] High prevalence of HIV among the population predisposes to increased fungal infections due to low immunity. One study has announced an evidently higher percentage of onychomycosis in HIV-positive patients with respect to general patients visiting dermatologic centers.[37] Goodman et al observed that the pervasiveness of dermatophytosis was four times higher among HIV infected people.[38]

Endonyx type was the most common clinical form of onychomycosis in our study followed by distal subungual onychomycosis (DSO) and total dystrophic onychomycosis (TDO). In this, patients presents with milky-white discoloration of the nail plate without hyperkeratosis or onycholysis. The dermatophyte responsible for endothrix type of hair invasion usually invades the nail.[39,40] We found very less cases of onychomycosis due to NDMs (10.16%) and *Candida albicans* (8.47%), this is possibly due to the fact that NDMs and Candida are the causative agents in tropical regions, whereas Botswana has a semi-arid climate with short rainy season. NDMs accounted for 100% toenail infections, whereas *Candida albicans* accounted for 80% fingernail infection and 20% toenail infection.

The treatment of onychomycosis is aimed at eradication of the causative organism and return to a normal appearance of a nail. Treatment of onychomycosis relies on factors like the patient's age and inclination of regimen (daily, weekly or monthly pulse therapy), the contaminating fungus and number of nails involved, level of nail association, whether toenails or fingernails are influenced and whether different medications are being taken.[41]

The first line systemic treatment for onychomycosis is griseofulvin, itraconazole, fluconazole and terbinafine.[42] An alternative topical treatment with 8% ciclopirox, 5% amorolfine and 40% urea plus 1% bifonazole can also be given but these are generally ineffective, with a failure rate of more than 60%, due to significant nail plate disease or nail matrix involvement. Concomitant nail debridement further increases the cure rates. Lasers and photodynamic therapies are also available. The long term cure is difficult to achieve in patients with onychomycosis.[42] Relapses and/or recurrences are common in these patients. The relapses are less common in patients treated with terbinafine compared to itraconazole.[42] Long term and continued treatment with efinaconazole 10% topical solution was found to be very effective and appeared to prevent relapses.[43] Efforts should be made for the accurate diagnosis and timely treatment of toenail onychomycosis as it does not typically cure itself and can trigger more infectious lesions in other parts of the body.[44] According to Mehregan and Gee treatment of onychomycosis should never be started without proper diagnosis of fungal infection.[45]

Conclusion

Efforts ought to be made for the precise diagnosis and timely treatment of onychomycosis as it does not ordinarily cure by itself and can trigger more infectious lesions in other parts of the body. The treatment of onychomycosis is aimed at the eradication of the causative organism (both clinical and mycological cure). HIV status should be investigated where multiple fingernails or toenails are involved.

Statement of ethics

The study was conducted in accordance with research ethics.

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Conflict of interest

The authors declare there is no conflict of interest.

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