

## The Impact of Negligence of Onychomycosis in Tropical Countries

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### Abstract

**Background:** Onychomycosis is a superficial anthropophilic fungal nail infection which can rapidly spread to other underlying keratinous tissues. High prevalence of onychomycosis in tropical countries is antecedent to other tinea infections due to the negligence and poor efficacy of anti-fungal drugs against the disease. Apparently, onychomycosis affects substantial quality of life and daily activities of human endeavors in endemic regions. The remarkable goals in management of onychomycosis include distorting the fungal pathogens and standard prevention of recurrence of the disease.

**Aim:** The purpose of this study was to carry out a systemic literature review on significant, prevalence, management and negligence of onychomycosis in tropical countries compared to other endemic areas.

**Method:** A Google search was conducted using “onychomycosis, Tinea unguium, Fungal nail infection and Fungal Neglected Tropical Disease”. The research was carried out from October to December, 2021, literature review from 2009 - 2020, meta-analyses, clinical and observational studies.

**Limitation:** We were not able to have full access to all literature review on Google search.

**Results:** Apparently, onychomycosis is a neglected tropical disease that should be included in the list of WHO portfolio as a Fungal Neglected Tropical Disease. Approximately 60% of finger nail and 80% of toe nail onychomycosis are caused by *Trichophyton rubrum* and *Trichophyton mentagrophytes*. *T. rubrum* is highly infectious anthropophilic dermatophytes producing arthrospores which have the potential ability to persist on the clothes, floor or shoes. In tropical countries, high prevalence of the dermatophytes causes fungal nail infection in subjects to their temperature, humidity, personal and environmental hygiene, insufficient health education and religious custom. Onychomycosis can be considered as an occupational hazard in agricultural activities, mining and those who walk bare footed in tropical countries.

**Conclusion:** *T. rubrum* is the most common etiological agent of fungal nail infections worldwide. Patient's health education, effective anti-fungal therapy and specific diagnostic techniques are paramount in accomplishing desirable end point of onychomycosis in the tropical countries and endemic areas.

**Keywords:** Onychomycosis; Anthropophilic; *T. rubrum*; Arthrospores; Anti-fungal drugs

### Introduction

In Africa, fungal diseases are not completely understood because these diseases are usually under reported or not reported at all. Insufficient or lack of human resources in clinical and diagnostic mycology in tropical countries influence the risk of high prevalence of fungal diseases.

Onychomycosis is a medical term used for any fungal infection of the finger and toe nail plate, unit, bed or matrix which often resulted into painful inflammation and decay of underlying keratinous tissues. The disease may predispose to rapid development of foot ulcers and diabetic foot syndrome [1-3].

Onychomycosis is worldwide in distribution with prevalence rates of 12% in tropical climates and 3% in temperate climate. The disease may likely remain fungal infection of modern civilization [4].

Onychomycosis is prevalent in tropical climates because of high temperature and humidity, low level of hygiene and health care, habit of walking barefoot and sharing common personal wears, low socioeconomic status, overcrowding and low level of health education in the communities [5].

In Fako division of Cameroon, diabetic patients are more prone of contracting onychomycosis compared to non-diabetic with prevalence rate of 50.7%. Distal and lateral subungual was frequently observed and approximately half of the diabetic in the population were contracted with the disease [6].

This could lead to diabetic foot syndrome and detrimental to their health status. *T. rubrum* was the common pathogen isolated, sensitive to miconazole, amphotericin B and ketoconazole and resistance to itraconazole and griseofulvin.

In Nigeria, a high prevalence of fungal toe nail infection was observed between ages 41 to 50 years and yeasts such as *Candida tropicalis*, *Candida parapsilosis*, *Candida pseudotropicalis* and *Torulopsis dattila* was predominant pathogen [7]. Studies revealed that most cases of onychomycosis are prevalence among farmers in rural areas of the age group of 40 to 49 years and the *Trichophyton rubrum* as the predominantly causative agent in the tropical regions [8].

In Tunisia, the prevalence of onychomycosis in their population was 77.4%, female were more vulnerable than male aged between 31 to 60 years [9]. However, the disease frequency may be due to negligence of the individuals who do not give importance to nail infections and can easily spread across. The presence of dormant arthroconidia in the nail unit or resistance fungal pathogens can serve as a reservoir for recurrent infections. And also misidentification of the causative fungal pathogens, inappropriate diagnosis and choice of anti-dermatophytic drugs can cause the high prevalence of the disease in Africa.

In Ethiopia, it was observed that the prevalence of onychomycosis was 60.4%, females were more vulnerable than men and the middle age group were more vulnerable to the disease. The isolation rates of molds, yeasts and dermatophytes were 32.3%, 33.3% and 44.7% respectively [10].

In Cameroon, the most common observed onychomycosis was distal and lateral subungual with prevalence rate of 8.8% in the population. However, *T. rubrum* and *T. violaceum* were the most frequent dermatophytes. A hot and humid climate of tropical and subtropical domicile enhances high prevalence of the disease [5].

The diseases are mainly caused by dermatophytes such as *Trichophyton mentagrophytes* and *Trichophyton rubrum* and yeasts such as *Candida guilliermondii*, *Candida krusei* and *Candida parapsilosis* [11,12].

The isolated moulds include *Onychocola canadensis*, *Fusarium species*, *Scopulariopsis brevicaulis*, *Aspergillus species*, *Scytalidium dimidiatum* and *Scytalidium hyalinum* [13].

In Africa, fungal infection of the nail is predominately caused by yeasts and among fungal infection that affect the nail unit, almost 50% are caused by dermatophytes [14,15].

According to the World Health Organisation (WHO) superficial fungal infection affect about 30% of the world population and about 25% to 65% of adults are asymptomatic carriers of the fungal infection [16]. Some studies revealed that 10% to 15% of individuals are contaminated with fungal infection in their lifetime [17].

Studies have revealed high prevalence cases of onychomycosis affecting vulnerable people and 51.3% in those that do not practice daily personal hygiene [18].

Causative agents of onychomycosis thrive better in warm, moist and dark domicile [19].

World Health Organization (WHO) reports that millions of dollars is being spent for the treatment of onychomycosis. The disease is contagious and often results from untreated superficial fungal infection and can spread from nail to other part of the body and invade deep layers such as dermis and hypodermis and that can spread to the lymph nodes, brain and blood stream causing deep infection [20]. For instances, onychomycosis can open the new route to secondary bacterial infections promoting foot ulcers in diabetic patients and immunosuppressed individuals [1].

Individuals infected with HIV have a high risk of developing Onychomycosis when their T-Lymphocyte count as 400 cells mm<sup>-3</sup> and fungal infections tend to affects all nails. However, proximal subungual Onychomycosis is a relatively indicator of HIV infection [21].

Diabetics are highly vulnerable to develop onychomycosis due to complication such as retinopathy and cataracts or obesity. Approximately 34% of all diabetics have onychomycosis, they frequently displays several risk factors related with increased prevalence of the disease [1].

This fungal infection is often neglected in tropical countries and cause serious mental distress, itching, pain, and affect the quality of life [22].

Patients with chronic fungal nail infection may experience psychological and social challenges due to the appearance of the nail. The disease can have certain negative consequences and can potentially restrict social lives and work. Patient education is paramount as pharmacologic therapy for controlling the recurrence of the disease. However, treating tinea pedis and tinea manuum can prevent the recurrence of onychomycosis because the dermatophytes or moulds infecting the stratum corneum may act as a reservoir for re - infection of the nail plate [23].

In Australia and New Zealand, *Candida spp*, *Acremonium spp*, and *Aspergillus spp* were found in 60% of the patients either as a contaminants, co-infection or secondary infection in the population [21].

Dermatophytes account for most (90%) cases of the fungal infection of the toenails and at least 50% of the infection of fingernail [22].

In U.S and western countries, onychomycosis causes an important health challenge with 12% increase in prevalence mostly affecting elderly people above 65 years of age in the population [19].

Fungal infection of the nail, in contrast to those at other body sites is potentially difficult to eradicate because of extremely poor efficacy of anti-fungal drugs.

**Epidemiology and risk factors**

The dermatophytes *Trichophyton mentagrophytes* and *Trichophyton rubrum* are the major cause of onychomycosis and were originated from west Africa and spread to North and South America and Europe in the late 19<sup>th</sup> and early 20<sup>th</sup> centuries [21].

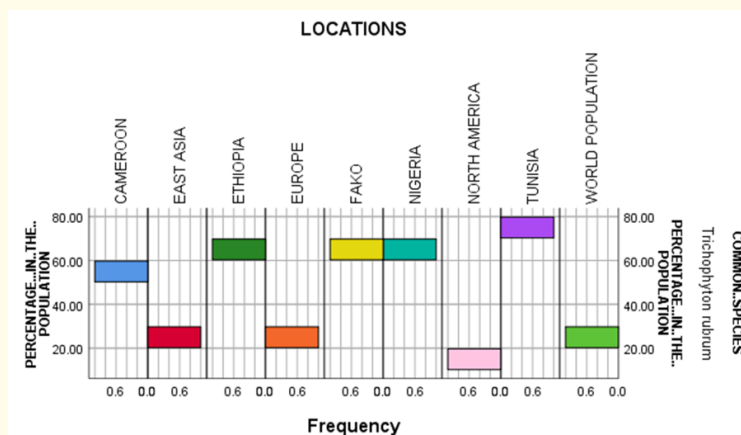
The associated use of occlusive foot wear and tight shoe, wars, invention of jumbo jet, the modern health movement, increased prevalence of urbanization, lockers room, obesity and migration in the early 20<sup>th</sup> century increased the incidence of fungal infection of the nail worldwide [21]. It has being reported that Onychomycosis is more prevalent in the elderly people and appears to occur more often in men than women. Some studies have revealed that aged 60 and 70 years above had approximately of 20% and 50% cases of Onychomycosis in the population [24].

Studies have shown that the prevalence of Onychomycosis increase with age because of suboptimal immune function, repeated nail trauma, inability to maintain good hand and foot hygiene, inability to cut the finger and toenails regularly, diabetes and poor peripheral circulation [25].

Fungal infection of the stratum corneum and nail are common whereas infection of the subcutaneous tissue and dermis by dermatophytosis is rare and uncommon life threatening. High prevalence and incidence associated morbidity make them an important public health challenge [26].

S/N	Locations	Common Species	Percentage
1	Nigeria	<i>Trichophyton rubrum</i>	63.60%
2	Tunisia	<i>Trichophyton rubrum</i>	77.40%
3	Ethiopia	<i>Trichophyton rubrum</i>	60.40%
4	Cameroon	<i>Trichophyton rubrum</i>	57.70%
5	Fako	<i>Trichophyton rubrum</i>	62.00%
6	Europe	<i>Trichophyton rubrum</i>	23.00%
7	East Asia	<i>Trichophyton rubrum</i>	20.00%
8	North America	<i>Trichophyton rubrum</i>	14.00%
9	World Population	<i>Trichophyton rubrum</i>	25.00%

**Table 1:** Summary of the prevalence of onychomycosis in some regions of the world [4-6,8,10,45,46].



**Figure 1:** Prevalence of the disease (Onychomycosis) in some tropical regions and other regions of the world [4-6,8,10,45,46].

### Classifications of onychomycosis

Dermatophytes are the predominant fungal pathogens of the disease however yeasts such as *Candida albicans* and non-dermatophyte molds may also be implicated. The infection depends on many factors especially environmental, climatic conditions, lifestyle and can be influenced by individual factors such as host defenses and age [27].

#### Distal and lateral subungual onychomycosis (DLSO)

DLSO is the most common type of the disease and usually caused by *Trichophyton rubrum*, *T. mentagrophytes*, *T. tonsurans*, and *E. floccosum* [28]. It is characterized by fungal invasion of the nail plate and bed at the hyponychium. The fungus moves from proximally via the underlying nail matrix. It produces mild inflammation resulting in subungual hyperkeratosis and parakeratosis. The formation of inflammation leads to thickening of the subungual region and onycholysis. The subungual region can potentially serve as a reservoir for non-dermatophyte mold and bacteria, giving the nail plate a yellowish brown pigmentation [28].

#### Proximal subungual onychomycosis (PSO)

PSO is a relatively uncommon type of onychomycosis in general population. *Fusarium* spp and *Trichophyton rubrum* are the major causative agents [29]. It occurs when dermatophytes invade the nail unit through the proximal nail via the cuticle region. The clinical presentation includes destruction of the proximal nail plate, leukonychia, proximal onychomycosis and subungual hyperkeratosis [30].

#### White superficial onychomycosis (WSO)

WSO is less common than DLSO approximately about 10% cases in population. It occurs when dermatophytes notably *Trichophyton mentagrophytes* invade the superficial layers of the nail plate directly. The infection may migrate via nail plate to infect the cornified layer of hyponychium and the nail bed. At this point, the nail becomes crumbly, soft and rough with minimal inflammation and occurs primarily in the toenails [30].

#### Total dystrophic onychomycosis (TDO)

TDO is used to describe end stage of fungal infection of the nail. The entire nail unit becomes dystrophic and thick [26].

### Diagnosis

Suspected onychomycosis can be observed via diagnosis typically clinical and mycological identification such as onycholysis, nail disfigurement and discoloration, hyperkeratosis and laboratory confirmation of fungal pathogens. The clinical feature of the diseased nail determine the site of sample collection [31]. In the laboratory, 40% of potassium hydroxide solution (KOH) will be added to the part of suspected onychomycosis sample. That will breakdown the keratin for fungal pathogens to be examined by direct microscopy [21]. Dermoscopy is a useful and highly effective tool, non-invasive and help to differentiate other nail infections from onychomycosis. It can also be used to locate the abrasion during sample collection for mycological identification [32]. Etiological agents of onychomycosis can be confirmed through direct microscopic and histopathological examination, culture, Polymerase Chain Reaction (PCR) assays [30]. Depending on the clinical features, nail clippings and scrapings are important sample to be collected [33]. A sterile blade and clipper should be used to collect subungual debris and full thickness of the nail plate [34]. PCR testing is considered to be highly specific and sensitive, rapidly and accurately for identification and amplification of fungal DNA fragments. However, PCR assay are relatively expensive and not widely available and that influence their use especially in the tropical climates [35].

Adequate nail samples should be collected in a standard mycological procedure and delivered to the laboratory for examination [34].

### Pathogenesis

Dermatophytes are fungal organisms that infect keratinized layer of the stratum corneum and utilize keratin as a source of nutrient for them to thrive. This allows them to colonise the keratinized tissue of the stratum corneum and its segments [30].

They are hyaline septated, the hyphae penetrate the nail and fungal cell produce keratinolytic proteases and penetrate living cells through keratinous tissues [28].

The ability of dermatophytes to adhere to epithelial cells has been incorporated to carbohydrate specific adhesions, expressed on the surface of microconidia [27].

At the surface of stratum corneum, long and thin fibrils attach fungal arthroconidia to keratinocytes while in the inner layer, arthroconidia express thin and short appendices on the surface [27].

And further, releasing proteases target to digest the keratin network into assimilable oligopeptides and secrete many metallo-endo-proteases and serine [36].

### Negative effects of onychomycosis

It consumes a sizeable proportion of funds in proper health care treatment. The patients may experience embarrassment in social and working place because they feel uncomfortable and unwilling to allow their affected hand or feet to be look at. The patients may be scared that they may transmit the fungal pathogens across their coworkers, friends or family members. The disease can create fear in the heart of patients which can leads to diminished self-esteem and avoiding interaction with the public. Long duration and lack of success in the treatment of the disease can cause patients to feel discourage or even to stop treatment. It discomforts patients to carry out work related task such as prolong standing, writing or typing which can lead to barrier to achieve work success [21].

### Predisposing factors of the disease

Old age, diabetes mellitus, down syndrome, hallux valgus, asymmetric gait nail unit syndrome, psoriasis, HIV infection, peripheral vascular impairment, peripheral neuropathies, sport activities, traumatic nail disorder and obesity [37-39].

### Prevention

Most dermatophytes thrive best in tropical regions because of relatively high temperature and humidity. Individuals should be advised to be washing their hand and feet thoroughly with soap and clean water and drying which apparently is the best approach. Sterilized hand gloves should be worn on any public functions. Finger and toenails should be clipped across so that the nail does not extend beyond the tip of the nails. Instrument used to cut nails should be disinfected regularly. Immersion of the hand and feet in water should be avoided [40].

### Treatment

Clinical and mycological confirmation of onychomycosis should be observed before treatment in order to avoid misdiagnosis, risk of the side effects of the medications and therapeutic failure [41]. Onychomycosis is difficult to treat or not completely cured because of the nature of deep-seated fungal nail infection and the disease may returns eventually [14]. This implies treatment failure and frequently been associated with high recurrent rate of 30% to 60% in treatment [42]. According to WHO, 4% of anti-fungal drugs that are prescribed may not be scientifically proven for standard treatment of the disease.

However, treatment of onychomycosis includes surgical avulsion of the diseased nail, anti-fungal chemical powder, topical or oral anti-fungal agents, laser therapy, and photodynamic therapy. The course of treatment of the fingernail infections is shorter compared to toenail fungal infection. The antifungal drugs used for the treatment of the disease may have side effect such as liver damage or drug interaction [43].

Recent available topical agents such as ciclopirox 8% and amorolfine 5% have low penetrating ability of approximately 5% while oral antifungal therapy such as terbinafine, itraconazole and fluconazole are considered the gold standard for the treatment of onychomycosis with high cure rates compared to available topical agents [30].

This low penetrating power can mainly be expressed to the inability of drugs or agents to penetrate through the nail plate and bed where the fungal infections take place. The extensive involvement of the entire nail unit, thickness, lateral fungal infection and pigmentation contribute to a poor response rate of treatment of the disease [44].

### Conclusion

Onychomycosis is a common nail disorder and often neglected in Africa. Fungal nail infections are uncommonly complain in general medical practice and dermatology consultations in tropical regions of the world. Dermatophytes usually invade healthy nails with the increasingly ageing in the population. Onychomycosis should be expected to become an emerging health problem as older people and immunosuppressed individuals are more prone to the disease. And further research should be carried out on prevalence, management and treatment of the disease in tropical regions.

### Recommendation

- Onychomycosis should be included in the list of WHO portfolio as a fungal neglected tropical disease.
- To avoid going barefoot in public and/or private places and keeping the foot or hand clean, dry and cool frequently.
- To promote health education on need to improve health and personal hygiene.
- To spray anti-fungal chemical inside shoes frequently.
- To comply with all treatment protocol for the proper management of the disease.

### Conflicts of Interest

The authors declare no conflict of interest.

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