

Onychomycosis: Etiology, diagnosis, and treatment

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Abstract

Background: Onychomycosis, although a common problem in all age groups, is often misdiagnosed and consequently under-treated. There is need for improved awareness and proper laboratory diagnosis to ensure effective therapy. **Objective:** To review the etiology, diagnosis, and treatment of onychomycosis. **Design:** Data sources from internet searches on AJOL and Pubmed conducted using the keywords "onychomycosis," fungal nail infections. **Setting:** Abia State University Teaching Hospital (ABSUTH), Aba, in South Eastern Nigeria. **Subjects:** A total of 38 articles and laboratory manuals. **Materials and Methods:** A total of 38 articles including laboratory manuals, published between 1974 and 2009, were selected and reviewed. **Results:** Onychomycosis is gradually increasing in the general population. The etiological agents differ from person to person and from place to place. **Conclusion:** There is need for proper laboratory diagnosis prior to institution of therapy. Effective therapy is with the use of systemic drugs with or without topical agents.

Key words: Diagnosis, Etiology, Onychomycosis, Treatment

INTRODUCTION

Onychomycosis is a fungal infection of finger and toe nails caused by dermatophytes, yeasts, or non-dermatophyte moulds.^[1,2] Onychomycosis represents about 30% of diagnosed superficial fungal infection and may involve any component of the nail unit including the nail matrix, nail bed, or nail plate.^[1] Onychomycosis, though not life-threatening (in immunocompetent individuals), can cause pain, discomfort, and disfigurement. It may also produce serious physical and occupational limitations. Psychosocial and emotional effects resulting from onychomycosis are widespread and may have a significant impact on quality of life.^[3] Onychomycosis is worldwide in distribution. Prevalence rates range from 2% – 3% in temperate climates to 12% in tropical climates.^[1,4-7] Prevalence rates in children are 30 times less than adults, ranging from 0%-0.2%.^[8]

The incidence of onychomycosis is increasing tremendously owing to such factors as ageing of the population, increasing number of immunocompromised and diabetic patients.^[9,10] In these group of people, infection could take on a serious turn. Predisposing factors include nail trauma, male gender, hyperhidrosis, peripheral vascular disease, poor hygiene, and tinea pedis.^[11] Others are increasing exposure to pathogens in public swimming pools and bathrooms, over exposing hands and feet to water, and the habit of wearing other people's shoes.^[5]

Onychomycosis is often identified by its appearance. However, other conditions and infections can cause problems in the nails that resemble onychomycosis. Confirmation must, therefore, be based on laboratory tests. This is important before treatment is commenced because treatment is long, expensive, and has side-effects associated with it.^[12] Even though the treatment of onychomycosis is difficult, it is important because onychomycosis does not resolve spontaneously.

This paper reviews the etiology, laboratory diagnosis, and treatment of onychomycosis.

Etiology of onychomycosis

The etiological agents of onychomycosis differs from place to place and even within the same place differs with the passage of time.^[13] The dermatophytes are the most common causes of onychomycosis worldwide. Onychomycosis caused by a

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dermatophyte is known as tinea unguium. In Nigeria, implicated dermatophytes include *Trichophyton rubrum*, *T. mentagrophytes T. soudanense*, *T. tonsurans*, *Epidermophyton floccosum*.^[6,7,8,14,15] Non-dermatophytes implicated as causes of onychomycosis in Nigeria are *Hendersonula toruloidea* and *Scytalidium hyalinum*.^[4] Non-dermatophytes that may cause infection include *Aspergillus sp*, *Acremonium sp*, *Fusarium oxysporum*, *Scopulariopsis brevicaulis*.^[10,16] *Emericella quadrilineata* has been implicated.^[17] Yeasts involved in onychomycosis are *Candida* species. The chief etiologic agent is *C. albicans*. Others are *C. parapsilosis*, *C. glabrata*, *C. guillemontii*, *C. krusei*, and *C. tropicalis*.^[10,18] Nail invasion by *Candida* is not common because the yeast needs an altered immune response as a predisposing factor to be able to penetrate the nail.^[1] Hence, *Candida* onychomycosis occurs as an opportunistic infection in HIV and diabetic patients.

Clinical presentations of onychomycosis

The main subtypes of onychomycosis are distal lateral subungual onychomycosis (DLSO), white superficial onychomycosis (WSO), proximal subungual onychomycosis (PSO) endonyx onychomycosis candidal onychomycosis, and total dystrophic onychomycosis (TDO).^[19]

Distal Lateral Subungual Onychomycosis (DLSO)

This is the commonest presentation and is characterized by invasion of the nail bed and underside of the nail plate. This results in subungual hyperkeratosis (thickening of the nail plate) and onycholysis (separation of the nail plate from the nail bed). Nail bed becomes cornified, and normal nail contour is lost.^[2] Both dermatophytes and non-dermatophytes are implicated.^[4,16]

White Superficial Onychomycosis (WSO)

This occurs when the fungi invade the superficial layers of the nail plate directly. It is characterized by the presence of white patches with distinct edges on the surface of the nail.^[19] The dermatophyte, *T. mentagrophytes* and non-dermatophyte moulds e.g. *Acremonium spp*, *Aspergillus terreus*, and *Fusarium oxysporum* have been implicated.^[16]

Proximal Subungual Onychomycosis (PSO)

Infection begins by the invasion of the cuticle and the ventral portion of the proximal nail fold and spreads to the newly forming nail plate. This results in of the subungual hyperkeratosis, proximal onycholysis, and destruction of the proximal nail plate.^[9]

Endonyx Onychomycosis (EO)

This is a variant of DLSO where fungi via the skin directly invade the nail plate. ¹ It presents as a milky white discoloration of the nail plate, but in contrast to DLSO, no evidence of subungual hyperkeratosis or onycholysis is present. It is caused by organisms that normally produce endothrix scalp infections e.g. *T. soudanense*.^[20]

Candidal Onychomycosis (CO)

It occurs in patients with chronic mucocutaneous candidiasis. *Candida sp* invade the nail plate directly to produce *Candida*

paronychia, *C. granuloma*, or *C. onycholysis*.^[21] *Candida* paronychia is the most common type marked by swelling and erythema of the proximal and lateral nail folds. It is also called a whitlow. *Candida granuloma* is uncommon and is characterized by direct invasion and thickening of the nail plate and associated paronychia. *Candida* onycholysis occurs when the nail plate separates from the nail bed. Distal subungual hyperkeratosis can be seen as a yellowish-grey mass lifting of the nail plate.

Total Dystrophic Onychomycosis (TDO)

This is total destruction of the nail plate. The entire nail becomes dystrophic and thickened. TDO is used to describe the end result of any of the above patterns of onychomycosis.

Diagnosis of onychomycosis

The diagnosis of onychomycosis consists of clinical and laboratory diagnosis.^[22] Clinical diagnosis is based on patient's history and physical examination of the infected nail. Onychomycosis accounts for about 50% of nail dystrophies; hence, other nail dystrophies must be ruled out.^[23] The differential diagnoses include trauma, Lichen planus, psoriasis, nail-bed tumor, perivascular disease, atopic dermatitis, contact dermatitis, yellow nail syndrome, idiopathic onycholysis, and onychogryphosis.

Onychomycosis must be confirmed by laboratory diagnosis before commencement of treatment. This is important to identify mixed infection and to optimize treatment.^[22,24]

Successful laboratory diagnosis begins with the collection of appropriate specimen. The method of specimen collections differs with the type of onychomycosis.^[2]

In cases of DSO, the specimen is collected from the nail bed as proximally as possible to the cuticle where the concentration of viable fungi is greatest. In cases of PSO, the specimen should be taken from the infected proximal nail as close as possible to the lanula. In cases of WSO, the white spots on the nail plate are scrapped and the outermost surface discarded. The white debris directly underneath is collected.^[25] For EO, discolored portions on the nail plate are scrapped directly. In *Candida* infections, the material closest to the proximal and lateral nail edges are obtained. If *Candida* onycholysis is suspected, scrapings of the infected nail bed and undersurface of the nail plate are taken. In cases of TDO, any abnormal area of the nail plate or bed can be used as specimen.^[1]

The specimen is divided into two parts, one for direct microscopy in 10% potassium hydroxide solution and the other, for culture using appropriate media.^[26-29] If neither microscopy nor culture yields a diagnosis, histological analysis using periodic acid-Schiff (PAS) staining will help determine whether pathogen is a fungus.^[30] PAS also helps to differentiate between dermatophytes and non-dermatophytes. To confirm that a non-dermatophyte is the causative agent and not a contaminant, the non-dermatophyte must be demonstrated consistently by repeated culture on two or more occasions.^[31]

Treatment of onychomycosis

Treatment of onychomycosis is very important, not only because they do not resolve spontaneously but they also spread to other nails and become reservoir for the infection of other people.^[9] Onychomycosis is difficult to treat due to the lengthy period the nail takes to grow, the hardness of the nail plate, and the location of the infection between the nail plate and the nail bed.^[32] However, newer drugs able to overcome these problems are available. Treatment options for onychomycosis are topical, systemic, and surgical. In choosing any option, the physician needs to consider the patient's age and health, the infecting organism, potential side effects and drug interactions of the various agents, cost of treatment, dosage schedule, and patient's compliance.^[2]

Topical agents available include 28% tioconazole solution with undecylenic acid (Trosyl), Amorolfine (Loceryl), and Ciclopirox in the form of nail lacquers.^[33]

Others are ketoconazole cream (Nizoral), terbinafine cream (Lamisil), and nystatin cream, which is only useful in *Candida* onychomycosis.^[9] Topical antifungal agents, however, have low efficacy in eradicating onychomycosis.^[24] They are usually only recommended when oral antifungals are contraindicated, when the patient prefers it, or in mild infections involving less than half of the nail (especially WSO). Topical agents are limited because they cannot penetrate the nails deeply enough. They are more active when used in combination with oral therapy.

Oral antifungal agents are more useful in the treatment of onychomycosis, this is because they go through the body to penetrate the nail plate.^[34] In the past, oral griseofulvin and ketoconazole were used.^[24,35] Griseofulvin requires 6 months to reach the distal plate of a fingernail and 12 months to reach the same site on a toenail. It disappears as early as 2 weeks after treatment is stopped. The use of ketoconazole is limited by occurrence of severe side effects and significant drug interaction. However, they have been replaced by newer agents, itraconazole (Sporanox capsules) and terbinafine (Lamisil tablets). These agents offer shorter treatment periods, higher cure rates, and fewer side effects.^[36] They are also fairly safe with fewer contraindications. These drugs reach the nail plate within 7-21 days of administration and remain active for several months after therapy is stopped. Itraconazole has a broad spectrum activity against dermatophytes, non-dermatophytes, and yeasts. Terbinafine is effective against dermatophytes and some moulds but less active against yeasts.^[37] Non-dermatophytes respond poorly to griseofulvin and ketoconazole.^[16] Onychomycosis due to *Candida* spp. can also be effectively treated with fluconazole (Diflucan).^[38]

The liver profile of the patient should be ascertained before, during, and after treatment since the drugs are to be taken for a long time.^[2]

Surgical procedures involve removing the nail surgically or chemically. Surgical nail removal is not often used because of the discomfort, cost, and possible nail disfigurement since

the distal nail bed may shrink and become dislocated dorsally. Chemical avulsion using urea ointment is a painless method and preferred to surgery.^[38]

CONCLUSION

In view of the increasing incidence of onychomycosis, prompt and proper diagnosis is inevitable. This will guide physicians to the best treatment option to effectively handle the infection. In addition, the patient should be properly informed of his role in treatment, which is compliance to chosen treatment and avoidance of conditions that predispose to infection.

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