

# Onychomycosis: A Comprehensive Review of Current Diagnostics and Therapeutics

**Mahefuz Attar\*, Ravi Kurhade, Wasim Bagwan, Muskan Shaikh**

MDA School of Pharmacy, Kolpa

## ABSTRACT

Onychomycosis is a common habitual fungal infection of the fingernails and toenails, counting for over to 50 of all nail diseases worldwide. It's primarily caused by dermatophytes, particularly *Trichophyton rubrum*, Thoughtnon-dermatophyte molds and provocations similar as *Candida* species may also be involved. Threat Factors include advanced age, diabetes mellitus, supplemental vascular complaint, immunosuppression, Nail trauma, and dragged exposure to wettish surroundings. Clinically, onychomycosis presents with nail Abrasion, thickening, fineness, subungual debris, and onycholysis, frequently leading to pain, functional Impairment, and reduced quality of life. Opinion relies on clinical assessment supported by laboratory Evidence using potassium hydroxide microscopy, fungal culture, histopathology, or molecular ways. Treatment options include topical and systemic antifungal agents, with oral curatives similar as terbinafine and itraconazole demonstrating the loftiest cure rates. Still, treatment is frequently dragged and associated with rush and implicit adverse goods. Arising curatives, including ray treatment and new antifungal agents, Show pledge but bear farther evaluation. Early opinion and applicable operation are essential to help Complications and ameliorate patient issues.

**Keywords:** Onychomycosis; Nail infection; fungal infection; Nail disease; Antifungal treatment; Diagnosis

## INTRODUCTION

Onychomycosis is one form of a habitual fungal infection affecting either the fingernails or toenails, which is the most common nail complaint, worldwide. Onychomycosis accounts for about 50 of all types of nail conditions and roughly one- third of all symptoms of superficial fungal skin infection. Although not generally life- hanging, onychomycosis has a large public health effect due to its ubiquitous nature, ongoing duration, frequent returns, and large negative impacts upon the case's quality of life. Dermatophytes are the primary agents that beget the condition, especially *Trichophyton rubrum*; to a lower extent, non-dermatophyte molds and other fomenters analogous to *Candida* species are also being honored as possible causes of this condition, particularly with fingernail infections and when individualities are immunocompromised. originally, the infection occurs at the distal(tip) or side(side) nail borders, and fleetly progresses throughout; it spreads to other factors of the nail unit (nail bed, nail plate, matrix), performing in nail health- related problems, similar as thinning or inordinate consistence, splitting or breaking,

onycholysis(separation), and disfigurement. There are several clinical subtypes of this condition that have been described, including distal subungual onychomycosis, superficial white onychomycosis, proximal subungual onychomycosis, endonyx onychomycosis, and total dystrophic onychomycosis. The global frequence of onychomycosis varies extensively, ranging from 2 to over 14, depending on geographic position, climate, individual criteria, and population studied. Its prevalence increases with advancing age and is told by multiple prepping factors similar as diabetes mellitus, supplemental vascular complaint, immunosuppression, nail trauma, inheritable vulnerability, and dragged exposure to wettish surroundings. Life factors, including the use of occlusive footwear and collaborative bathing installations, also contribute to complaint transmission. With the growing population and the rising frequence of habitual systemic conditions, the burden of onychomycosis is anticipated to increase further. Although frequently considered an ornamental problem, onychomycosis can lead to significant physical discomfort, pain, secondary bacterial infections, and functional impairment,

**Relevant conflicts of interest/financial disclosures:** The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.



particularly in senior cases and those with comorbidities. In cases with diabetes, undressed onychomycosis may increase the threat of bottom ulcers and cellulitis, potentially leading to serious complications. Also, nail defect can beget cerebral torture, social embarrassment, and reduced tone-regard, emphasizing the significance of effective operation. Opinion of onychomycosis remains grueling. Clinical appearance alone is inadequate due to imbrication with other nail diseases similar as psoriasis, lichen planus, and traumatic nail dystrophy. Laboratory evidence using potassium hydroxide (KOH) microscopy, fungal culture, histopathology, or molecular individual ways is recommended before initiating treatment. Still, limitations similar as low perceptivity, prolonged culture times, and limited vacuity of advanced individual tools can complicate accurate opinion in routine clinical practice. Operation of onychomycosis is frequently dragged and complex, taking a acclimatized approach grounded on complaint inflexibility, causative organism, nail involvement, patient comorbidities, and threat of medicine relations. Treatment options include topical antifungal agents, systemic antifungal remedy, combination rules, and spare physical modalities similar as ray remedy and photodynamic remedy. Despite advances in antifungal pharmacotherapy, treatment issues are constantly sour, with high rates of relapse and reinfection. Factors similar as poor nail penetration of topical agents, adverse goods of systemic medicines, patient non-adherence, and antifungal resistance contribute to remedial failure. There continues to be a great deal of ongoing exploration regarding onychomycosis (a fungal nail infection) because of the high prevalence and frequency as well as the unique circumstances related to this complaint, which can have considerable public health counteraccusations. To ameliorate the clinical issues in cases with this complaint, it's essential for healthcare professionals to have a complete understanding regarding the causes of onychomycosis, the individual threat factors that a case may have, the colorful forms of treatment presently available, and any new treatment options that may be developed in the future. The purpose of this composition is to give a broad and simplified overview of onychomycosis, with a primary focus on recent advancements in the opinion and treatment,

gaps in current literature regarding onychomycosis, and the unborn direction of exploration in this area.

## 2. Epidemiology of Onychomycosis

Onychomycosis is the most common nail complaint worldwide and accounts for roughly 20 – 50 of all nail conditions and up to 30 of superficial fungal infections. Its frequencies varies extensively according to age, geographic region, climate, life factors, and comorbid conditions.

### 2.1 Global frequencies

The estimated global frequencies of onychomycosis ranges from 5 – 12 in the general population, with advanced rates reported in developed countries. Population- grounded studies from Europe and North America report frequencies rates between 6 – 14, whereas lower rates are generally observed in children and adolescents.

### 2.2 Age and coitus Distribution

Onychomycosis is generally a complaint of grown-ups and aged individualities. Frequencies increases markedly with age, affecting up to 20 – 50 of individualities over 60 times and further than 50 of those over 70 times in some studies. Factors contributing to age- related vulnerability include reduced nail growth, bloodied supplemental rotation, accretive nail trauma, and immunosenescence.

### 2.3 Geographic and Environmental Factors

Geographic variation is told by climate and socioeconomic conditions. Advanced frequencies rates are reported in temperate and sticky climates, which favor fungal growth. Civic populations and industrialized regions demonstrate increased frequencies, likely affiliated to occlusive footwear, collaborative bathing installations, and sports- related conditioning. Onychomycosis, scientifically known as fungal nail infection and affecting toenails, has a variety of causes. Fortunately, fungi are the least common sources of this disease; dermatophytes make up the inviting number of cases.

### 2.4 Factors Impacting the Development of Onychomycosis



There are multiple factors associated with both the host and the terrain that place individualities at increased threat of developing onychomycosis

- Diabetes mellitus
- Supplemental vascular complaint
- Immunocompromise (HIV, organ transplant)
- Psoriasis and other nail plate conditions

### 3. Etiology and Causative Agents of Onychomycosis

#### A. Etiology

Onychomycosis is a habitual fungal infection of the fingernails or toenails caused by keratin-digesting fungi. The infection occurs when fungi foray the nail plate, nail bed, or nail matrix, generally through minor trauma, dragged humidity exposure, or compromised host defenses. Prepping factors include advanced age, diabetes mellitus, immunosuppression, supplemental vascular complaint, poor nail hygiene, and frequent exposure to wetish surroundings.

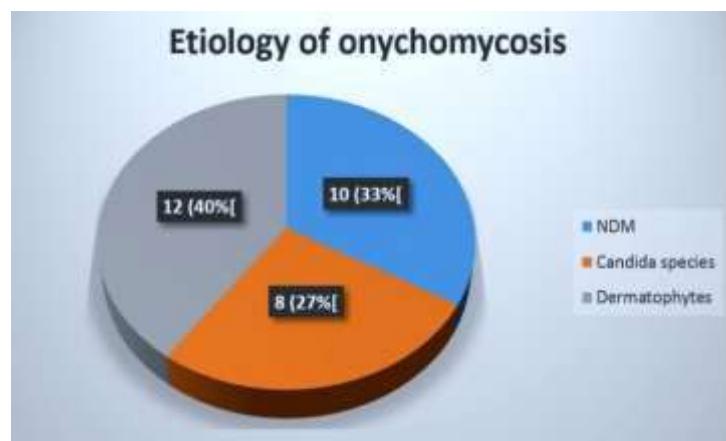


Figure 1. Etiology of onychomycosis

#### B. Causative Agents

The causative organisms of onychomycosis are astronomically classified into three major groups:

##### 1. Dermatophytes (Most Common)

- These fungi account for approximately 80–90% of cases and have a high affinity for keratin.
- *Trichophyton rubrum* (most common worldwide)
- *Trichophyton mentagrophytes*
- *Epidermophyton floccosum*

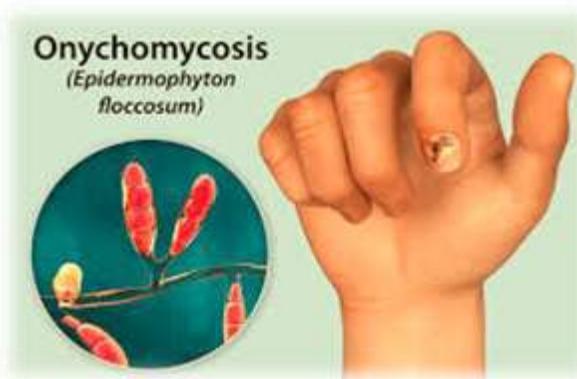


Figure 2. (Epidermophyton)

##### 2. Non-Dermatophyte Molds

- These organisms are increasingly recognized, especially in immunocompromised patients and in tropical climates.
- *Aspergillus* species

- *Scopulariopsis brevicaulis*
- *Fusarium* species
- *Acremonium* species

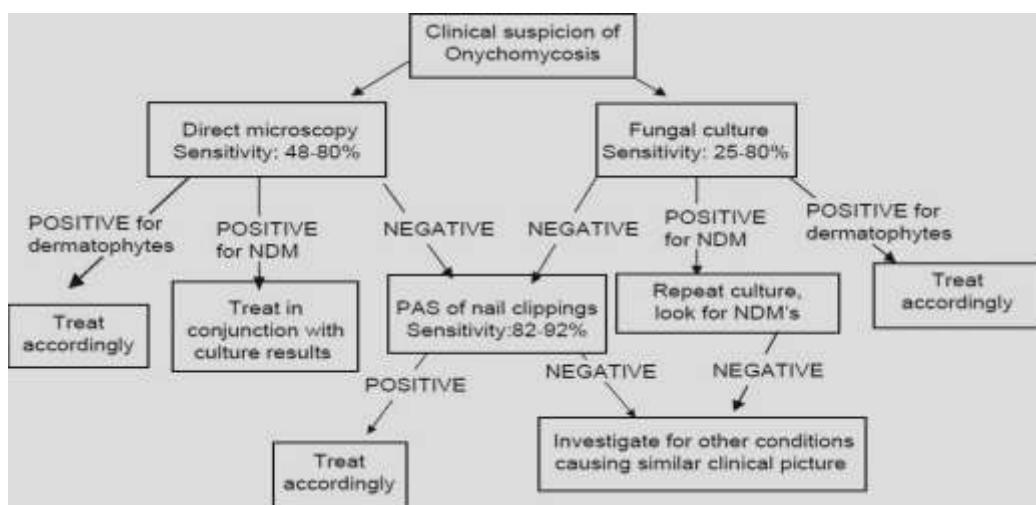
##### 3. Yeasts



- More commonly associated with fingernail infections, particularly in individuals with chronic exposure to water.
- *Candida albicans*

- *Candida parapsilosis*
- *Candida tropicalis*

#### 4. Pathogenesis



**Figure 3. Pathogenesis of onychomycosis**

A. Fungal infections generally do through micro-injury, cracks or trauma to nails. Fungal infections generally start at either the distal edge of the nail or nail bed or beneath the cuticle. Contributing factors to fungal infections poor hygiene, occlusive footwear, diabetes, immunosuppression, and supplemental vascular complaint.

B. Adherence of fungi to nails occurs because dermatophytes produce adhesins and keratinases, which give the capability of fungi to cleave to and/ or degrade keratin. Nail keratin is hard, compact, and avascular; thus it's veritably hard for vulnerable cells to reach it.

C. The fungi foray the nail plate, nail bed, and/ or nail matrix, and produce enzymes (keratinases) to degrade keratin, as well as proteases and lipases to degrade structural proteins. This causes abnormal nail growth (thickened, soft, and or lifted) and/ or separation of nail from nail bed.

- Thickening and subungual debris
- Pain or secondary bacterial infection in severe cases

#### Summary of Medium

1. Trauma/ entry → fungi pierce the nail
2. Adhesion → fungi attach to keratin
3. Keratin declination → nail plate destruction via enzymes
5. Clinical changes → abrasion, thickening, and onycholysis.

#### 5. Classification of Onychomycosis

Onychomycosis is classified predicated on the route of fungal incursion, clinical appearance, and anatomical point of nail involvement.

##### 5.1 Distal and Side Subungual Onychomycosis (DLSO)

- Most common form
- Fungal incursion occurs from the distal or lateral nail edge
- Involves the nail bed and underside of the nail plate

#### Causes

- Nail abrasion (white, unheroic, brown)



**Figure 4. Distal and Side Subungual Onychomycosis (DLSO)**

**Clinical features**

- Onycholysis
- Subungual hyperkeratosis

- Pusillanimous – white or brown bruise
- Generally caused by *Trichophyton rubrum*

**5.2 White Superficial Onychomycosis (WSO)**



**Figure 5. White Superficial Onychomycosis (WSO)**

- Fungal infection of the superficial nail plate
- Appears as white, chalky patches on the nail face
- Nail becomes soft and crisp
- More common in toenails

- Common pathogens *Trichophyton mentagrophytes*

**5.3 Proximal Subungual Onychomycosis (PSO)**



**Figure 6. Proximal Subungual Onychomycosis (PSO)**

- Infection begins at the proximal nail fold
- Spreads distally beneath the nail plate

- Constantly associated with immunosuppression (e.g., HIV infection)

**5.4 Endonyx Onychomycosis**



**Figure 7. Endonyx Onychomycosis**

- Direct incision of the nail plate without involvement of nail bed or nail fold
- Nail appears
- Milky white
- Lamellar splitting
- The Common pathogens are *Trichophyton soudanense*, *T. violaceum*

## 6. Sign and symptoms of onychomycosis

Onychomycosis (fungus infection of the nail) is a chronic infection. A fungus invades an affected area of the nail unit (matrix, nail plate, or nail bed), resulting in changes to that area. Many host factors (including route of infection) as well as the fungus organism determine what you may see clinically.

### Clinical Features of Conditions Involving the Nails:

- Nail Color Change - nails are yellow, white, brown, or black
- Nail Thickening - each nail will have a thickened appearance and may be long
- Subungual Hyperkeratosis
- Nail is brittle and crumbly
- Nail Plate Separation or Onycholysis (nail bed from nail)
- Unevenness of Nail Surface; reduced ability to see through nail
- Pain or discomfort with severe conditions; predisposition to secondary infection with bacteria

## 7. Management and Treatment Strategies

### 7.1 Systemic (Oral) Antifungal Therapies

Systemic antifungal agents are considered the gold standard for moderate to severe onychomycosis due to their superior nail penetration and higher cure rates.

#### A. Terbinafine

- **Class:** Allylamine
- **Mechanism of action:** The epoxidase inhibition and causes ergosterol, which kills the fungus.
- **Dosage:**
  - Fingernails: Take accurate dose 250 mg/day for 6 weeks
  - Toenails: Take accurate dose 250 mg/day for 12 weeks
- **Advantages:**
  - Highest mycological and clinical cure rates
  - Fungicidal activity
- **Limitations:**
  - Hepatotoxicity risk
  - Drug–drug interaction

#### B. Itraconazole

- **Class:** Triazole
- **Mechanism of action:** The Inhibits fungal cytochrome in P450-dependent on lanosterol demethylation
- **Dosage:**

Take Continuous 200 mg/day for 12 weeks for daily. Take Pulse therapy 200 mg twice daily for 1 week/month (2–3 pulses) time to time

- **Advantages:**

- Broad antifungal spectrum

- Pulse dosing improves adherence

- **Limitations:**

- Cardiotoxicity risk
- Extensive drug interactions
- Variable bioavailability

Low nail penetration

### C. Fluconazole

- **Class:** Triazole

- **Dosage:** Take accurate dose 150–300 mg once a week for 6–12 months

- **Spectrum:** Yeasts > dermatophytes

- **Advantages:**

- Good tolerability
- Convenient dosing

- **Limitations:**

- Lower cure rates
- Long treatment duration

### B. Efinaconazole

- **Class:** Triazole

- **Formulation:** 10% topical solution

- **Mechanism:** Inhibits ergosterol synthesis

- **Advantages:**

- Enhanced nail penetration
- No nail debridement required

- **Limitations:**

- High cost
- Prolonged therapy

### C. Tavaborole

- **Class:** Oxaborole

- **Formulation:** 5% topical solution

- **Mechanism:** Inhibits fungal protein synthesis

- **Advantages:**

- Low molecular weight improves penetration

- **Limitations:**

- Moderate efficacy
- Expensive

## 7.2 Topical Antifungal Therapies

Topical therapy is indicated for mild to moderate onychomycosis, superficial disease, or in patients contraindicated for systemic treatment.

### A. Amorolfine

- **Class:** Morpholine derivative

- **Composition:** 5% nail polish

- **Mechanism:** Prevents the production of ergosterol

- **Application:** Once or twice weekly

- **Advantages:**

Broad-spectrum activity

Minimal systemic absorption

- **Limitations:**

Long treatment duration (6–12 months)

## 7.3 Combination Therapy

A strategy of using both oral antifungal medication (e.g. tablets) and topical antifungal treatment (e.g. creams or ointments) can have several advantages for treating nail fungus including:

- Greater overall success rates
- A lower chance of developing drug-resistance to the antifungal medications
- A shorter course of treatment
- This combination therapy can be especially useful for people with severe, recurrent and/or resistant toenail fungus.



**Table no.1 – Medication and their therapy, route, duration, spectrum, major limitation.**

Therapy	Route	Duration	Spectrum	Major Limitations
Terbinafine	Oral	6-12 weeks	Dermatophytes	Hepatotoxicity
Itraconazole	Oral	Pulse/Continuous	Broad	Drug interactions
Fluconazole	Oral	Long –term	Yeasts	Low cure rate
Amorolfine	Topical	6-12 months	Broad	Poor penetration
Ciclopirox	Topical	Daily	Broad	Low efficacy
Efinaconazole	Topical	Long-term	Dermatophytes	Cost

## 8. Combination therapy of onychomycosis

Therapy aims to enhance antifungal efficacy by:

- Improving drug penetration
- Targeting fungi through multiple mechanisms of action
- Reducing treatment duration and relapse rates

### 8.1 Systemic + Topical Antifungal Therapy

#### a. Oral Terbinafine + Topical Antifungals

Antifungal therapy for nails can be administered through a combined system.

- This includes both oral (terbinafine) and topical (amooral-fine/ciclopirox) routes of antifungal administration.
- The justification is that systemic antifungal agents (e.g., terbinafine) work at the level of the blood; topical antifungals are applied to the nail plate.

#### b. Oral Itraconazole + Topical Antifungals

Itraconazole + Topical Antifungal Medications

- Pulse Itraconazole plus Amorphine
- Pulse Itraconazole plus Ciclopirox

**Advantages:** Broader range of antifungal effect and can be effective against non-dermatophytic or mixed causative organisms.

**Use in practice:** Patients who cannot tolerate Terbinafine and who have onychomycosis associated with Candida.

## 8.2 Topical Antifungal Combinations

#### a. Sequential or Concurrent Topical Therapy

Topical Therapy - Sequential or Concurrent.

#### Examples:

Efinaconazole + Tavaborole

#### Rationale:

Combination therapy with antifungal topical agents having different penetration profiles and antifungal mechanisms may increase the likelihood of complete nail bed eradication.

#### Limitations:

Few high-quality randomized controlled trials have been completed; therefore, concurrent therapy is primarily reserved for the treatment of mild disease or as maintenance therapy.

### 8.3 Antifungal Therapy + Mechanical or Chemical Nail Debridement

#### A. Antifungal + Mechanical Debridement

Mechanical Debridement + Antifungal

- **Advantage:** Enhances topical medication penetration by lowering fungal load and nail thickness.
- **Signs:** Dystrophic, thickened nails

#### B. Antifungal + Chemical Avulsion

**Application:** Urea softens and removes infected nail portions, followed by topical or systemic antifungal therapy

**Outcome:** Improved clinical response in severe hyperkeratotic onychomycosis



**Table no.2 – Combination therapy and their indication, advantages and limitation.**

Combination strategy	Indication	Advantages	Limitations
Oral + Topical	Moderate –severe disease	Higher cure rates	Cost, compliance
Topical + Debridement	Thick dystrophic nails	Improved penetration	Requires expertise
Antifungal + Laser	Refractory cases	Non-invasive adjunct	Variable efficacy
Induction + Maintenance	High relapse risk	Lower recurrence	Long duration

## 9. Emerging and novel treatment

### 9.1 Novel Topical Antifungal Agents

Recent advances have led to the development of newer topical antifungal formulations with enhanced nail penetration and broader antifungal spectra.

#### A. Efinaconazole

Efinaconazole (a triazole antifungal drug) is extremely less affinity for keratin and can rapidly/easily penetrate the toenail. Efinaconazole works by blocking the activity of the enzyme which converts lanosterol to ergosterol, lanosterol 14-alpha-demethylase. When this enzyme is blocked, the production of ergosterol in the nails cannot occur. Clinical research has shown that efinaconazole is very effective for complete cure rates in individuals with mild to moderate distal/lateral subungual onychomycosis compared to traditional topical therapies.

#### B. Tavaborole

Tavaborole is an antihistamine that is derived from boron and works to inhibit the production of proteins by preventing leu-tRNA synthetase from producing proteins inside the body. Because of its small size, this medication has the ability to easily penetrate through the nails. Thus far, data indicates that Tavaborole has a good safety profile, as well as moderate efficacy (especially in instances where a systemic therapy (i.e. oral) cannot be administered).

#### C. Luliconazole

Luliconazole, an imidazole antifungal, exhibits potent activity against dermatophytes with prolonged retention in keratinized tissues. Emerging evidence suggests its potential role in topical onychomycosis therapy, particularly when combined with nail debridement.

## 9.2 Advanced Drug Delivery Systems

Improving drug delivery through the dense keratinized nail plate remains a major therapeutic challenge. Novel delivery strategies are being explored to enhance antifungal efficacy.

#### A. Nanotechnology-Based Systems

Nanoparticles, nanoemulsions, and liposomal formulations enhance drug solubility, stability, and penetration. Antifungal agents such as terbinafine, itraconazole, and fluconazole encapsulated in nanocarriers have demonstrated improved transungual delivery and antifungal activity in preclinical studies.

#### B. Medicated Nail Lacquers with Permeation Enhancers

Modern nail lacquers incorporate chemical permeation enhancers such as urea, salicylic acid, and thioglycolic acid to disrupt nail keratin structure, allowing better drug diffusion. These formulations offer sustained drug release and improved patient adherence.

## 9.3 Physical and Device-Based Therapies

Device-based approaches provide non-pharmacological alternatives or adjuncts to conventional antifungal treatments.

#### A. Laser Therapy

Laser treatment modalities, including Nd: YAG (1064 nm), diode, and CO<sub>2</sub> lasers, act by generating heat that disrupts fungal cell walls and inhibits fungal growth. Laser therapy offers advantages such as minimal systemic side effects and short treatment sessions; however, variability in clinical efficacy and lack of standardized protocols remain limitations.

#### B. Photodynamic Therapy (PDT)



Photodynamic therapy involves the application of a photosensitizing agent followed by light activation, producing reactive oxygen species that destroy fungal cells. PDT has shown promising results, particularly in refractory onychomycosis, although multiple treatment sessions are often required.

#### **9.4 Biological and Immunomodulatory Approaches**

Novel biological strategies aim to enhance host immune responses or directly target fungal pathogens.

##### **A. Antimicrobial Peptides**

Antimicrobial peptides exhibit broad-spectrum antifungal activity through membrane disruption and immunomodulation. Synthetic and naturally derived peptides are currently under investigation for topical application in onychomycosis.

##### **B. Probiotics and Microbiome-Based Therapy**

Modulation of the nail and skin microbiome using probiotic organisms represents an emerging therapeutic concept. Certain bacterial strains have demonstrated antagonistic activity against dermatophytes in vitro.

##### **9.5 Combination Therapies**

Combining topical agents with systemic antifungals, laser therapy, or mechanical nail debridement has shown enhanced treatment outcomes. Combination regimens may reduce treatment duration, minimize drug resistance, and lower relapse rates, particularly in severe or recalcitrant cases.

##### **9.6 Future Perspectives**

Innovative onychomycosis solutions stress not only targeting drug delivery but also reduced adverse effects associated with systemic drugs and patient adherence. Current investigations focus on the use of nanotechnology, new antifungal targets and immunotherapies offer the potential for enhanced efficacy and sustained success. Before any of these therapies can be relied upon for long-term success, they must be tested in large, prospective randomized clinical studies for both safety and long-term efficacy.

#### **10. Antifungal Resistance in Onychomycosis**

##### **10.1 Introduction**

Onychomycosis is a habitual fungal infection of the nail unit, counting for roughly 50 of all nail diseases worldwide. It's primarily caused by dermatophytes, particularly *Trichophyton rubrum* and *Trichophyton interdigitale*, but non-dermatophyte molds (NDMs) and provocations similar as *Candida* spp. are decreasingly intertwined. Although antifungal remedy — both topical and systemic — has significantly bettered clinical issues, antifungal resistance has surfaced as a growing challenge, contributing to treatment failure, rush, dragged remedy, and increased healthcare costs. Antifungal resistance in onychomycosis can be natural (primary) or acquired (secondary) and is told by microbial, pharmacological, host, and environmental factors.

##### **10.2 Etiological Agents and Resistance Trends**

###### **A. Dermatophytes**

The fungus causing onychomycosis has the largest group of all user agents considered dermatophytes - *Trichophyton rubrum*, *Trichophyton interdigitale* and *Epidermophyton floccosum*. Dermatophyte species that were thought to be generally responsive to antifungal drugs, particularly alkyl aspartates and triazoles, have recently demonstrated some resistance, especially to terbinafine, which has been the traditional first-line therapy when treating systemically.

###### **B. Non-Dermatophyte Molds (NDMs)**

Molds that are not derived from dermatophytes are considered to be Non-Moulds (NDMs). Examples include: Non-Dermatophyte Molds (NDMs) are a similar group of molds that include *Fusarium* spp., *Scopulariopsis brevicaulis*, and *Aspergillus* spp. These molds show a high degree of natural resistance to many conventional antifungal agents, resulting in low clinical success and high relapse rates.

###### **D. Yeasts**

*Candida albicans* and non-albicans *Candida* species are more common in fingernail onychomycosis and immunocompromised hosts. Resistance to azole



antifungals, particularly itraconazole and fluconazole, is well proved in these species.

### 10.3 Mechanisms of Antifungal Resistance

#### A. Resistance to Allylamines (Terbinafine)

Allylamine Resistance (Terbinafine)

Resistance mechanisms:

- Mutations that change the SQLE gene (point mutations) resulting in decreased binding of the drug
- Over expression of SQLE
- Activation of alternate pathways for the production of sterols

#### B. Resistance to Azoles

Azoles act on the enzyme lanosterol 14- $\alpha$ -demethylase (Erg11). There are several mechanisms that will allow for resistance to azole: genetic mutations (within the Erg11 gene); over-expression of Erg11; up-regulation of efflux pumps (ATP-binding cassette (ABC) transporters and major facilitator super-family (MFS)); and biofilm formation. Cross-resistance can occur between azole antifungals such as itraconazole, fluconazole, and voriconazole.

#### C. Resistance to Polyenes and Other Agents

Although polyenes (e.g., amphotericin B) are not routinely used in onychomycosis, resistance mechanisms include

- differences in ergosterol content
- Oxidative stress response adaption

Newer agents similar as efinaconazole, tavaborole, and luliconazole show lower resistance rates, but long-term data are limited.

## 11. Prevention and Patient Education in Onychomycosis

Onychomycosis is a chronic fungal infection of the nail unit with high recurrence rates even after successful treatment. Effective prevention strategies and comprehensive patient education are essential components of disease management, aiming to reduce transmission, improve treatment outcomes, and prevent relapse.

### 11.1 Prevention of Onychomycosis

#### A. Practicing Individual Hygiene

- Clean and dry your hands and feet thoroughly and often (especially find dry all the gaps between your toes) to reduce the amount of moisture conducive to fungal development.
- Keep your nails (both hands and feet) short (cut straight and not rounded) and clean to avoid microtrauma.
- Do not over-trim your nails or cuticles or bite at your nails, as this will compromise the barrier of the nails and allow access to the fungus through the damaged barrier.

#### B. Footwear and Clothing Practices

Opt for breathable footwear (leather or mesh type). AVOID wearing occlusive types of shoes for long periods, so try to wear a new pair of socks each day, especially after going to the gym or working out. Moisture-wicking socks will wick moisture from your feet and will help reduce the risk of damaging your toenails because they will also avoid wearing too many shoes that fit too tightly.

#### C. Environmental and Behavioural Measures

1. Always wear proper foot protection (i.e. flip-flops/sandals) while attending public exercise facilities (as exercise facilities are likely to spread foot infections) - changing rooms and showers are very common locations where foot infections are likely to be spread.
2. Do not share personal items from someone else. (E.g. washcloth, socks, nail clippers, nail files, etc.). These items harm to affect the human like bacteria and/or fungi on them...

#### D. Nail Care and Cosmetic Practices

To promote appropriate sterilizing methods for use in nail salons while avoiding establishments that don't practice good hygiene.

- discourage the use of artificial nails, nail wraps, and prolonged wear of nail polish because these products



can contain moisture leading to an increased risk of growing fungi.

- Advise on the use of antifungal nail polishes or prevention topical antifungal agents for high risk persons.

## 11.2 Patient Education in Onychomycosis

Patient education is critical for improving adherence to treatment, reducing recurrence, and enhancing long-term disease control.

### A. Understanding the Disease

Patients should be educated in:

The fungal infection etiology of onychomycosis and its chronic, slowly progressive nature. The prolonged duration of treatment required due to slow nail growth.

### B. Treatment Adherence and Expectations

They should highlight the necessity of finishing prescribed topical or systemic antifungal therapy, even when there is an early indication of improvement. They should educate the client about the differences between mycological cure, clinical improvement, and complete nail regrowth.

### C. Nail and Skin Care Education

The Encourage routine in inspection of nails and surrounding a skin for early signs and symptoms of infection.

Advising gentle nail care practices and avoidance of cosmetic procedures during treatment. Reinforcing the importance of concurrent treatment of tinea pedis and household contacts if necessary. The following are some of the roles healthcare professionals have in terms of education and prevention:

## 12. Impact of Onychomycosis on Quality of Life

There is accumulating evidence to show the detrimental effects of onychomycosis (a toenail fungus infection) on the quality of life of patients who have this disease; however, it is still viewed primarily as a cosmetic problem. Onychomycosis affects your physical comfort, mental health, social activity,

ability to perform work, and overall health status. The impact of these factors on a patient depends on the severity/extensity of the infection, the number of infected nails, any pre-existing medical conditions, and the characteristics of the individual.

### A. Physical and Functional Impairment

Onychomycosis can cause functional and pain issues, usually more severe for toenails. Thick nails, brittle nails, and dystrophic nails can create problems such as: Pain with walking, standing, or when wearing shoes; difficulty with cutting nails and maintaining foot hygiene; an increased risk of bacterial infections due to potential for secondary infections; deformities of the nails can cause discomfort related to pressure on the nails. Mobility may be affected if severe conditions occur; for example, subungual hyperkeratosis and thickening of the nail plate can create limitations of mobility in elderly individuals and/or individuals who have diabetes or have peripheral vascular disease. Functional limitation may decrease daily activity and increase risk for physical inactivity.

### B. Psychological and Emotional Impact

Onychomycosis is a fungal nail infection that can negatively impact the patient's emotional and mental well-being and frequently goes unrecognized/considered. Patients experience feelings of embarrassment and self-consciousness regarding their fingernails and also suffer from low self-esteem related to dissatisfaction with their body image. Patients also feel concerned about nail appearance, nail odour, and fear of transmitting the infection to others. Nail changes that are seen (especially in the case of fingernails) may lead to embarrassment and/or social stigmas for the patient. In addition, many patients are discouraged, feel powerless, and fatigued by the lengthy time period since they were diagnosed with onychomycosis, the repeated recurrences of their onychomycosis, the length of time it has taken to witness results from treatment by their health care provider. Research has been completed by various researchers using validated instruments (i.e., Dermatology Life Quality Index (DLQI), NailQoL) to measure the impact of onychomycosis on the patient's overall quality of life. When surveyed, patients reported having greatly reduced quality of life due to



their onychomycosis and demonstrated a strong statistical association between a high quality of life (score) and onychomycosis severity and duration.

### C. Social and Interpersonal Consequences

Onychomycosis (known as nail fungus) has been shown to decrease an individual's ability to participate in leisure and social activities, which typically involve some degree of social interaction with others. People with onychomycosis will often limit certain social interactions including:

- \* People Participate in social situations where they may show their feet (such as at the pool, gym, or beach)
- \* The touching someone else (by shaking hands) who has an infection (fungus) on their nails.
- \* Getting nail care services or using public nail care services.

### D. Occupational and Professional Impact

This condition can lead to work-related problems because it may affect people whose jobs involve hand appearance or where they frequently interact with the public, such as in healthcare, food service, hospitality and cosmetic industries. Patients may also face challenges including:

- Lack of confidence about professional abilities
- Embarrassment about working in the workplace
- Having to have limited duties at work due to hygiene regulations

Untreated or more severe cases of nail fungus may also lead to absenteeism from work and/or loss of productivity.

### 13. Challenges in the Management of Onychomycosis

Onychomycosis is a long-lasting fungal infection of the nail unit caused mainly by dermatophytes and NDMs, as well as yeast. Even though the condition is frequently diagnosed, it has not been easy to treat due to pose significant clinical, diagnostic, treatment, and patient-related issues. Because of these reasons, up to 40% of patients will fail to respond adequately to their prescribed treatments, resulting in high rates of relapse and dissatisfaction among patients.

## 13.1 Diagnostic Challenges

### A. Clinical Mimicry

Onychomycosis has similar appearances to multiple non-fungal nail disorders — including:

- Psoriasis, Lichen planus, Traumatic onychodystrophy
- The misdiagnosis have potentially result in incorrect antifungal treatment, and prevention and unnecessary medication exposure and/or delay in proper treatment.

### B. Low Sensitivity of Conventional Tests

The Standard diagnostic methods include potassium hydroxide (KOH) microscopy, fungal culture, and histopathology. However:

- KOH preparation is operator-dependent and lacks species identification
- Fungal cultures have low sensitivity (30–60%) and long turnaround times

### C. Limited Access to Advanced Diagnostics

Molecular techniques such as PCR offer higher sensitivity and rapid results but are limited by:

- High cost
- Lack of standardization

## 13.2 Pathogen-Related Challenges

### A. Diversity of Causative Organisms

Dermatophytes (e.g., *Trichophyton rubrum*) are by far the most common cause of dermatophyte infections, however, more cases of a variety of other fungi are also being seen including:

- Non-dermatophyte molds such as (eg. *Scopulariopsis*, *Fusarium*).
- Yeasts such as (eg. *Candida* spp.)

### B. Emerging Antifungal Resistance

Dermatophytes are becoming increasingly resistant to the antifungal agent terbinafine due to:

- Changes to genes coding for the squalene epoxidase enzyme



- Extensive, widespread use of antifungals without a proven need or for an extended duration

### 13.3 Nail Anatomy and Drug Penetration

The nail plate is prepared of densely packed keratin, which limits drug penetration.

Challenges include:

- Poor permeability of topical antifungals
- Reduced efficacy in cases with thickened or dystrophic nails

### 13.4 Therapeutic Challenges

Both terbinafine and itraconazole are effective oral antifungal medications; however, their use is limited by:

- 1) Hepatotoxicity
- 2) Drug interactions (primarily in elderly patients)
- 3) Contraindication in people with liver disease, pregnancy or polypharmacy. As such, oral antifungal medications are usually not suited to high risk groups.

## 14. Future Perspectives and Research Directions in Onychomycosis

Onychomycosis is still a common, long-lasting, difficult-to-treat nail condition that produces a large picture of physical, psychological, and economic damage. Even though antifungal medications have improved, we continue to have problems with high rates of relapse, long treatment times, inadequate drug penetration to the nail, antifungal resistance, and issues with diagnosing the condition accurately, which all prevent us from having the best possible outcome in treating people with onychomycosis. As a result, more research should be done to improve the way we diagnose onychomycosis, treat people who have onychomycosis, help people who have onychomycosis stay on their treatment, and develop prevention strategies using a multidisciplinary approach.

### 14.1 Advances in Diagnostic Techniques

A critical aspect of managing onychomycosis comes with the promptness of diagnosis; ensuring a timely diagnosis will allow for the delivery of quality

treatment for patients who have developed fungal nail infection. The diagnostic methods to determine the presence of this type of infection include KOH microscopy, culture, and histopathology. All three of these methods have been reported to have variable sensitivity, lengthy turnaround times to receive results, and variability from one operator to another. In the not-too-distant future, four areas of research are expected to focus on improving the methods of diagnosing onychomycosis.

1) Molecular diagnostics (e.g., PCR and NGS) should rapidly and accurately identify dermatophytes, non-dermatophytes, and yeasts down to the level of species;

2) Point-of-care testing should be developed using microfluidic devices and/or biosensors so clinicians can produce results indicating the presence of fungus during a patient's visit;

### 14.2 Novel Antifungal Agents and Drug Targets

Fungistatic action, drug interactions, liver toxicity, and resistance have restricted current antifungal treatments. As a result, the focus of future research on antifungal therapy will likely include the development of:-- Prima facie anti-fungal agents for use against fungal target pathways such as mitochondrial function, heat shock proteins, and signalling mechanisms-- Improved squalene epoxidase and lanosterol demethylase inhibitors with improved selectivity and reduced toxicity-- Antifungal peptides and immunomodulatory agents that may improve the immune system's response to a fungus through mechanisms that do not directly attack the fungus-- Antifungal treatments against fungal bioluminescent in nail tissue that are contributing to the chronicity of every type of treatment.

### 14.3 Advanced Drug Delivery Systems

Treating onychomycosis presents a major difficulty due to the fact that drugs have a poor ability to penetrate the nail plate. To improve penetration of antifungals into the nail, several research projects are being conducted to identify novel drug delivery systems including:

1. Nanotechnology-based formulations (liposomes, nanoparticles, nano-emulsions, solid lipid



nanoparticles) that will increase antifungal penetration and provide sustained-release characteristics.

2. Drug penetration enhancement methods (iontophoresis, laser-assisted delivery, microneedle therapy, and nail plate perforation).
3. The use of both a topical and a systemic medication as a combined treatment to achieve the synergy between both forms of medications while maintaining minimal exposure to systemic medication.

#### 14.4 Laser and Device-Based Therapies

Patients who are unsuited for antifungal medications may be considered for laser therapies. However, evidence of their use can be mixed and would justify further studies on:

- (1) Standardizing the parameters of lasers, including through the purpose of wavelength, pulse duration, fluence, and treatment intervals;
- (2) Examining the exact antimicrobial and immune effects of lasers through mechanistic investigation;
- (3) Developing a combination treatment regimen with lasers as well as other antifungal or debridement formulations, which might increase efficacy; and
- (4) Long-term outcomes and recurrence of disease by way of future studies on these options.

#### CONCLUSION:

Onychomycosis is still considered the most common fingernail and toenail disease in the world and presents the patient as well as the community with many challenges. Chronicity of onychomycosis, high frequency of recurrence, and adverse effects on quality of life define this disease as a public and clinical health challenge. The key to managing this disease successfully results from addressing the barriers to appropriate management including delayed diagnosis, poor patient adherence, drug lack of coordination, and newly emerging resistance of antifungals. Accurate identification of the microorganisms responsible for onychomycosis, providing an early intervention and creating an individual treatment plan will provide optimal outcomes in managing onychomycosis. More effective agents than existing antifungals in addition to the use of combination or non-pharmacological procedures for persons with contraindications to

systemic antibiotics have developed as novel treatment modalities for onychomycosis. Future research will address the need for improvements in diagnostic accuracy, an understanding of the mechanisms of resistance, and the development of safer and more effective therapeutic agents for the reduction of the burden of disease and the recurrence of onychomycosis. The successful management of onychomycosis must use a comprehensive approach, focusing on the patient as the center of care.

#### REFERENCE

1. Gupta A.K., Versteeg S.G., Shear N.H. Confirmatory testing prior to initiating onychomycosis therapy is cost-effective. *J. Cutan. Med. Surg.* 2018; 22(2):129–141. doi: 10.1177/1203475417733461.
2. Gupta A.K., Mays R.R., Versteeg S.G., Shear N.H., Piguet V. Update on current approaches to diagnosis and treatment of onychomycosis. *Expert Rev. Anti-Infect. Ther.* 2018; 16(12):929–938. doi: 10.1080/14787210.2018.1544891.
3. Angelo T., Borgheti-Cardoso L.N., Gelfuso G.M., Taveira S.F., Gratieri T. Chemical and physical strategies in onychomycosis topical treatment: A review. *Med. Mycol.* 2017; 55(5):461–475. doi: 10.1093/mmy/myw084.
4. Bodman MA, Krishnamurthy K. Onychomycosis. StatPearls [Internet]. aTreasure Island (FL): StatPearls Publishing; 2019 Jan- 2019 Jan 5.
5. Gupta A.K., Sibbald R.G., Andriessen A., Belley R., Boroditsky A., Botros M., et al. Toenail onychomycosis - A Canadian approach with a new transungual treatment: Development of a clinical pathway. *J. Cutan. Med. Surg.* 2015;19(5):440–449. doi: 10.1177/1203475415581310.
6. Joyce A., Gupta A.K., Koenig L., Wolcott R., Carviel J. Fungal diversity and onychomycosis: An analysis of 8,816 toenail samples using quantitative PCR and next-generation sequencing. *J. Am. Podiatr. Med. Assoc.* 2019;109(1):57–63. doi: 10.7547/17-070.
7. Thomas J., Jacobson G.A., Narkowicz C.K., Peterson G.M., Burnet H., Sharpe C. Toenail onychomycosis: An important global disease burden. *J. Clin. Pharm. Ther.* 2010;35(5):497–519. doi: 10.1111/j.1365-2710.2009.01107. x.



8. Youssef A.B., Kallel A., Azaiz Z., Jemel S., Bada N., and Chouchen A., et al. Onychomycosis: Which fungal species are involved? Experience of the Laboratory of Parasitology-Mycology of the Rabta Hospital of Tunis. *J. Mycol. Med.* 2018; 28(4):651–654. Doi: 10.1016/j.mycmed.2018.07.005.

9. Fike J.M., Kollipara R., Alkul S., Stetson C.L. Case report of onychomycosis and tinea corporis due to *Microsporum gypseum*. *J. Cutan. Med. Surg.* 2018; 22(1):94–96. doi: 10.1177/1203475417724439.

10. Lipner S.R., Scher R.K. Onychomycosis: Clinical overview and diagnosis. *J. Am. Acad. Dermatol.* 2019; 80(4):835–851. Doi: 10.1016/j.jaad.2018.03.062.

11. Pang S.M., Pang J.Y.Y., Fook-Chong S., Tan A.L. Tinea unguium onychomycosis caused by dermatophytes: A ten-year (2005-2014) retrospective study in a tertiary hospital in Singapore. *Singapore Med. J.* 2018;59(10):524–527. doi: 10.11622/smedj.2018037.

12. Sato T., Kitahara H., Honda H., Katsukawa F., Hiruma M., Yaguchi T. Onychomycosis of the middle finger of a Japanese judo athlete due to *Trichophyton tonsurans*. *Med. Mycol. J.* 2019;60(1):1–4. doi: 10.3314/mmj.18-00012.

13. Solís-Arias M.P., García-Romero M.T. Onychomycosis in children. A review. *Int. J. Dermatol.* 2017;56(2):123–130. doi: 10.1111/ijd.13392.

14. Bombace F., Iovene M.R., Galdiero M., Martora F., Nicoletti G.F., D'Andrea M., et al. Non-dermatophytic onychomycosis diagnostic criteria: an unresolved question. *Mycoses.* 2016;59(9):558–565. doi: 10.1111/myc.12504.

15. Bongomin F., Batac C.R., Richardson M.D., Denning D.W. A review of onychomycosis due to *Aspergillus* species. *Mycopathologia.* 2018;183(3):485–493. doi: 10.1007/s11046-017-0222-9.

16. Hirose M., Noguchi H., Yaguchi T., Matsumoto T., Hiruma M., Fukushima S., et al. Onychomycosis caused by *Aspergillus subramanianii*. *J. Dermatol.* 2018;45(11):1362–1366. doi: 10.1111/1346-8138.14616.

17. Hon K.L., Leung A.K. Alopecia areata. Recent Pat. Inflamm. Allergy Drug Discov. 2011;5(2):98–107. doi: 10.2174/187221311795399291.

18. Kimura U., Hiruma M., Kano R., Matsumoto T., Takamori K., Suga Y. Onychomycosis caused by *Scopulariopsis brevicaulis*: The third documented case in Japan. *J. Dermatol.* 2019;46(5): e167–e168. doi: 10.1111/1346-8138.14677.

19. Martínez-Herrera E.O., Arroyo-Camarena S., Tejada-García D.L., Porras-López C.F., Arenas R. Onychomycosis due to opportunistic molds. *An. Bras. Dermatol.* 2015;90(3):334–337. doi: 10.1590/abd1806-4841.20153521.

20. Matsuyama Y., Nakamura T., Hagi T., Asanuma K., Sudo A. Subungual onychomycosis due to *Aspergillus niger* mimicking a glomus tumor: A case report. *Biomed. Rep.* 2017;7(6):532–534. doi: 10.3892/br.2017.994.

21. Mohanty P., Dash S., Mohapatra L., Jain M. Total dystrophic onychomycosis due to *Syncephalastrum racemosum* - A rare cause and its novel treatment option. *Indian Dermatol. Online J.* 2019;10(2):171–173. doi: 10.4103/idoj.IDOJ\_155\_18.

22. Moreno G., Arenas R. Other fungi causing onychomycosis. *Clin. Dermatol.* 2010;28(2):160–163. doi: 10.1016/j.cldermatol.2009.12.009.

23. Noguchi H., Hiruma M., Miyashita A., Makino K., Miyata K., Ihn H. A case of fingernail onychomycosis due to *Aspergillus flavus*. *Med. Mycol. J.* 2016;57(2): E21–E25. doi: 10.3314/mmj.57. E21.

24. Piraccini B.M., Alessandrini A. Onychomycosis: A review. *J. Fungi (Basel)* 2015;1(1):30–43. doi: 10.3390/jof1010030.

25. Pontini P., Gorani A., Veraldi S. Onychomycosis by *Paecilomyces lilacinus*. *G. Ital. Dermatol. Venereol.* 2016;151(6):706–709.

26. Pote S.T., Khan U., Lahiri K.K., Patole M.S., Thakar M.R., Shah S.R. Onychomycosis due to *Achaetomium strumarium*. *J. Mycol. Med.* 2018;28(3):510–513. doi: 10.1016/j.mycmed.2018.07.002.

**HOW TO CITE:** Mahefuz Attar\*, Ravi Kurhade, Wasim Bagwan, Muskan Shaikh, Onychomycosis: A Comprehensive Review of Current Diagnostics and Therapeutics, Int. J. Sci. R. Tech., 2026, 3 (2), 165-180. <https://doi.org/10.5281/zenodo.18638470>

