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ONYCHOMYCOSIS INSIGHTS INTO PATHOGENESIS, DIAGNOSTIC APPROACHES, AND EVOLVING TREATMENT STRATEGIES

***Rupali Pawar, Shailesh Pawar, Prem Pokale, Yash Chavhan, Anand Kamble, Dr. Rahul Bijwar**

Jagadambha Institute of Pharmacy and Research, Kalamb, Yavatmal, Maharashtra, India-445401.

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***Corresponding Author**
Rupali Pawar
Jagadambha Institute of Pharmacy and Research, Kalamb, Yavatmal, Maharashtra, India-445401.

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ABSTRACT

A large percentage of people worldwide suffer from onychomycosis, a prevalent chronic fungal infection of the nail unit, especially the elderly and those with weakened immune systems. Although yeasts and non-dermatophyte molds also play a role in its genesis, dermatophytes like Trichophyton rubrum are the main culprits. Fungal invasion of the nail plate, bed, and matrix causes the infection, which results in nail dystrophy, thickness, and discolouration. Diagnosis remains challenging due to the slow growth of fungi and variable clinical presentations; however, advances such as polymerase chain reaction (PCR), dermoscopy, and reflectance confocal microscopy (RCM) have improved detection accuracy. Current treatment strategies include topical and systemic antifungal agents, combination regimens, and emerging modalities like laser and photodynamic therapy, aimed at enhancing cure rates and reducing relapse. To reduce recurrence, preventive measures including early treatment, footwear, and hygiene are crucial. The pathophysiology, diagnostic techniques, and developing therapeutic approaches in the management of onychomycosis are highlighted in this review, which also emphasizes the necessity of ongoing research to maximize results, overcome treatment resistance, and lower relapse.

KEYWORDS: Diagnosis, Onychomycosis, Pathogenesis, Fungal.

1. INTRODUCTION

Onychomycosis, a chronic fungal infection of the fingernail or toenail bed, is commonly encountered in primary care. Onychomycosis is not just a cosmetic problem. If untreated, it can cause pain, discomfort, and physical impairment, negatively impacting quality of life. This article provides a summary of the best available patient-oriented evidence on the diagnosis and management of this condition Onychomycosis, a chronic fungal infection of the fingernail or toenail bed, is commonly encountered in primary care.

Onychomycosis is a common fungal infection of the nails, especially toenails. It causes nail discoloration, thickening, and separation from the nail bed (onycholysis).[1-2] Though often seen as a cosmetic issue, it can lead to discomfort, bacterial infections, and emotional stress especially in older adults, diabetics, and people with weak immune systems.

Onychomycosis (fungal nail infection) is not a life-threatening disease and it is primarily a cosmetic problem by causing disfigurement. It may as a reservoir of cutaneous and systemic infection. It is caused by three groups of fungal agents namely dermatophyte molds (DM), non-DM (NDM) and yeasts. Role of dermatophytes in onychomycosis is well-established.[3]

The main causes are dermatophyte fungi like *Trichophyton rubrum* and *T. mentagrophytes*, but yeasts (*Candida*) and molds (e.g., *Aspergillus*) can also be involved. These fungi invade the nail and may form biofilms, making treatment harder.

Onychomycosis affects about 10% of the population worldwide. This rate increases to 20% in those over 60 and up to 50% in those over 70. Risk factors include aging, diabetes, poor circulation, immune problems, and nail injuries.[4-9]

Treatment is difficult due to slow nail growth, poor drug penetration, and antifungal resistance. Options include oral antifungals (terbinafine, itraconazole), topical treatments (efinaconazole, ciclopirox), and newer therapies like laser and photodynamic therapy.[10]

Onychomycosis is a common, contagious fungal infection of the nails that causes them to become thickened, discolored, brittle, and separated from the nails.

Epidemiology and Prevalence:- Onychomycosis is a common fungal nail infection that affects approximately 10% of the general population. Its prevalence increases significantly with age, rising to 20% in individuals over the age of 60 and up to 50% in those over 70.

Several factors contribute to the development of onychomycosis, including aging, diabetes, peripheral vascular disease, immunosuppressive conditions, nail trauma, The condition is more frequently observed in males and predominantly affects the toenails due to slower nail growth, reduced blood circulation, and greater exposure to moisture and trauma.[11-12]

Clinical Important/Feature:- Nail discoloration (yellow, white, brown), Nail thickening and brittleness, Onycholysis (nail detachment), Subungual debris, Pain and discomfort in severe case.

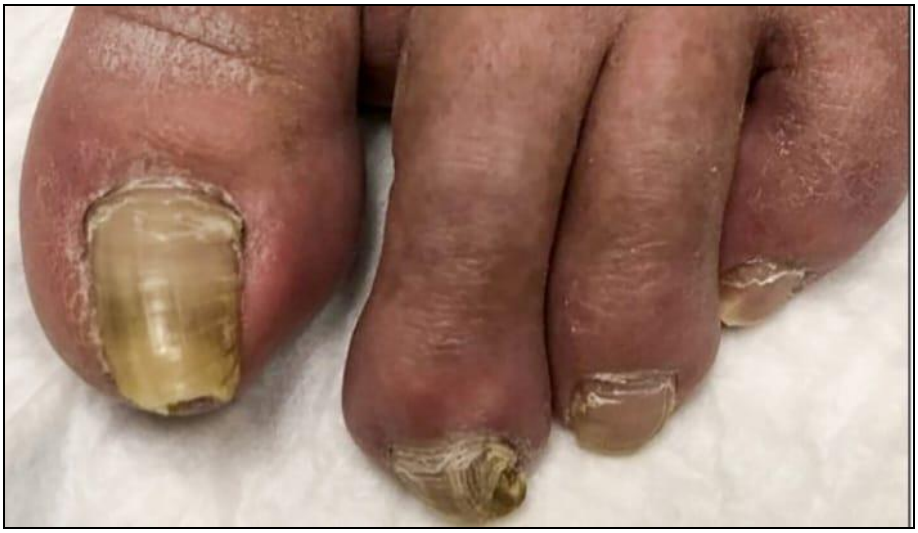

Fig. 1: Nail plate is entierly infected with fungi causing it to become brittle and prone to splitting, a condition known as onychomycosis.[13]

2. ANATOMY OF NAIL INFECTION

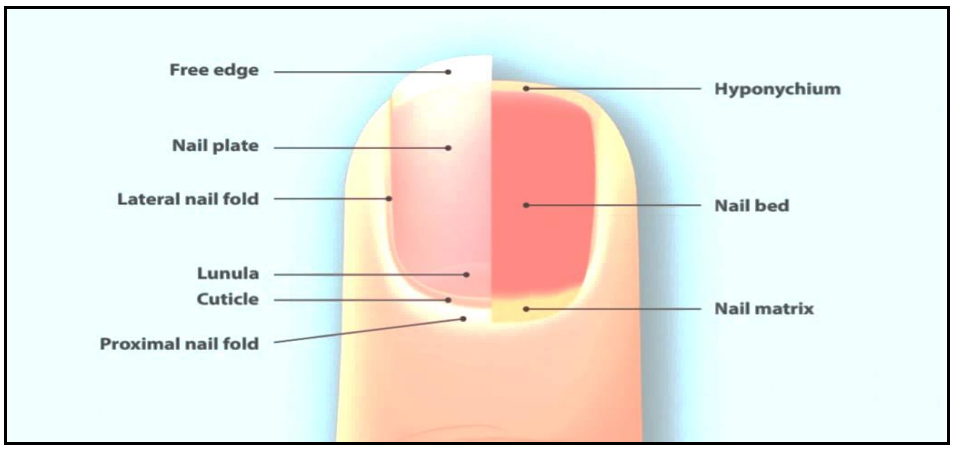

Fig. 2: Anatomy of Nail.

A review of the anatomy of the nail unit and the process of nail growth may be helpful in understanding the pathogenesis of dermatophytic fungi in the nail unit. A diagram of the nail

unit is presented in.[14] It consists of the following structures: proximal and lateral folds, cuticle, matrix, nail plate(commonly called the nail), nail bed, and hyponychium. The cuticle is the horny layer of the proximal nail fold; it consists of modified stratum corneum and protects the nail matrix from infection.[15] The nail matrix is the growth center of the nail. As the nail grows, cells of the nail matrix divide, differentiate, and keratinize and are incorporated into the nail plate. The distal, visible part of the matrix looks like a half moon and the lunula. The matrix extends approximately 5 mm proximally beneath the proximal nail fold. The nail plateis the largest structure of the nail unit and grows by sliding forward over the nail bed[16] whereupon the distal end become free of the nail bed. The hyponychium, the most distal component in the nail bed, is composed of epidermis that includes a granular layer similar to that seen in plantar and volar surfaces. Fingernails grow at a rate of 2 to 3 mm per month, and toenails grow at a rate of 1 mm per month. Therefore, it takes about 6 months to replace a fingernail and between 12 and 18 months to replace a toenail. This rate of growth is often decreased in the presence of peripheral vascular disease and onychomycosis and in the elderly.[17]

3. PATHOGENESIS OF ONYCHOMYCOSIS

Onychomycosis develops when fungal organisms attack and grow in the **keratinized tissues** of the nail unit. Fungal invasion of the nail begins with adhesion of fungal spores to the nail surface,[18-19] followed by penetration through the nail plate using keratin-degrading enzymes. Dermatophytes such as Trichophyton rubrum and T. mentagrophytes digest keratin to gain nutrients and invade deeper layers. The nail's limited immune defense and slow growth allow the fungi to persist, making onychomycosis a chronic infection.[20-21]

- **Fungus Enters the Nail:-** Fungi enter through small cuts, nail cracks, or surrounding skin. (especially if there's athlete's foot).
- **Fungi Start to Grow**:- They grow in the nail bed or under the nail plate, feeding on keratin (a protein in nails).
- **Nail Becomes Infected**:- The fungus grows, it damages the nail, causing: Thickening, Discoloration (yellow, white, or brown), Crumbly or brittle texture, Nail lifting (onycholysis).
- **Fungi Avoid Immune System**:- Some fungi form protective layers that make them hard to kill and help them hide from the immune system.

- **Infection Becomes Chronic**:- Slow nail growth, poor blood supply, and weak immune defence make it hard to clear the infection. The infection can long time or come back after treatment.[22-23]

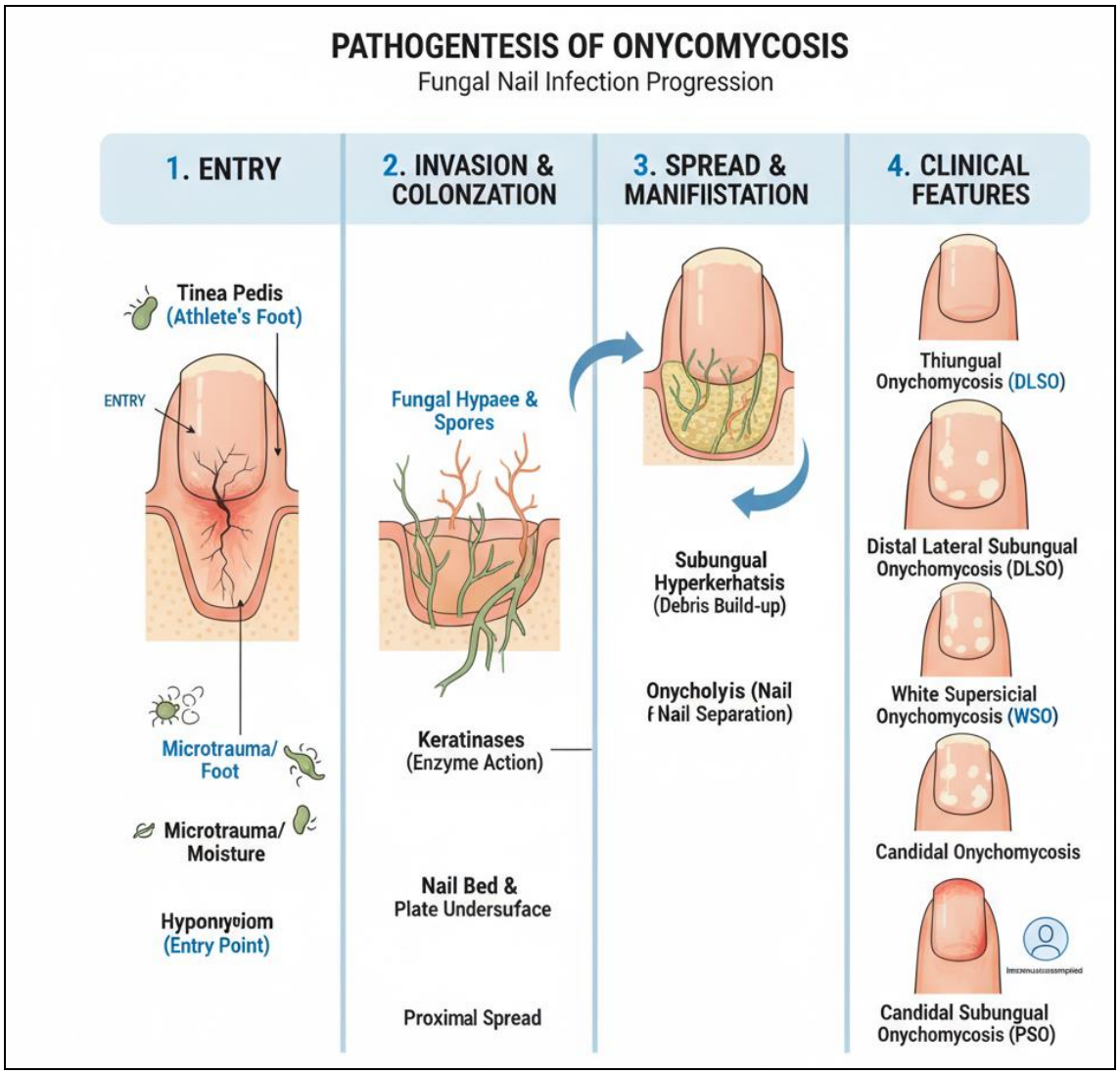

Fig. 3: Pathogenisis of onychomycosis.

Causing Agent :- Onychomycosis is caused by **fungal organisms** that attack the nail unit There are three main types of fungi responsible.

1. **Dermatophytes (Most Common Cause)**:- Responsible for ~90% of toenail infections, These fungi feed on keratin in nails.

Common species:- Trichophyton rubrum (most common)

2. **Yeasts:-** More common in **fingernail infections**, especially in people with chronic wet hands or immune suppression.

Common species:- Candida albicans

3. **Non-Dermatophyte Molds (NDMs):-** Found in **soil and the environment**, often seen in tropical regions, Typically affect nails that are already damaged or diseased.

- *Common species:- Aspergillus spp.*

Table 1: Common Etiological Agents of Onychomycosis.

Type	Common Species	Common in
Dermatophytes	T. rubrum, T. mentagrophytes	Toenails
Yeasts	Candida albicans	Fingernails
Non-dermatophyte mold	Aspergillus spp	Damaged nails, tropics

4. **PREDISPOSING FACTORS**

Several factors increase the risk of developing onychomycosis. These include advancing age, poor peripheral circulation, diabetes mellitus, obesity, and immune suppression. Repeated nail trauma, wearing tight or non-breathable footwear, and exposure to moist environments also promote fungal growth**.**[24]

4.1 Host Factors

These are personal or biological conditions that increase susceptibility: Age – More common in elderly due to slower nail growth and reduced immunity. Gender – Slightly more prevalent in males.Genetic predisposition – Some families have higher susceptibility.

Reduced immunity – Seen in HIV/AIDS, malignancy, or immunosuppressive therapy. Systemic diseases – Diabetes mellitus ,Peripheral vascular disease Hyperhidrosis (excess sweating).[25]

4.2 Environmental Factors

These involve surroundings and exposure risks

Warm, humid environments – Promote fungal growth.

Use of occlusive footwear – Reduces ventilation and traps moisture.

Public places – Pools, locker rooms, salons (where fungi can spread).

Occupational exposure – Farmers, miners, or athletes are at higher risk.[26]

4.3Nail-Related (Local) Factors: These directly affect the nail's defense or structure:Trauma to nails – Repeated minor injuries allow fungi to invade, Nail deformities. Poor nail hygiene – Accumulation of dirt and moisture aids fungal colonization.[27]

5. CLASSIFICATION

There are four major clinical presentations of onychomycosis.

- Distal and lateral subungual onychomycosis
- Proximal subungual onychomycosis
- Superficial white onychomycosis
- Total dystrophic onychomycosis

5.1 Distal and lateral subungual onychomycosis

Distal subungual onychomycosis (DSO) is the most common type of nail fungus infection. It starts under the nail tip (hyponychium) and spreads toward the nail root through the nail bed and nail matrix.[28] This causes mild inflammation, thickening of the skin under the nail (subungual hyperkeratosis), and separation of the nail from the nail bed (onycholysis).[29] The space under the nail can then trap bacteria and mold giving the nail a yellowish-brown color The main fungus responsible for DSO is Trichophyton rubrum, but T. mentagrophytes, T. tonsurans, and Epidermophyton floccosum can also cause infection. DSO can affect both fingernails and toenails, but toenail infections are much more common.[30-31]

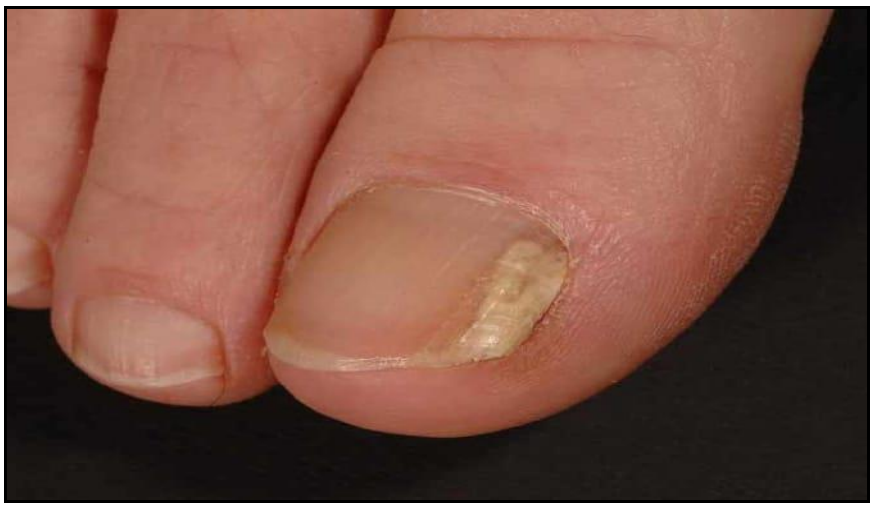

Fig. 4: Distal and lateral subungual onychomycosis.

5.2 White Superficial onychomycosis

White superficial onychomycosis (WSO) is a less common type of nail fungus infection, making up about 10% of all onychomycosis cases.[32] It happens when certain fungi attack the surface layers of the nail plate directly. As the infection progresses, it can spread deeper into the nail and reach the nail bed and skin under the nail (hyponychium).WSO appears as white, powdery spots or patches (“white islands”) on the nail surface.[33] These spots may merge and

spread, making the nail rough, soft, and crumbly . Because the infection affects only the dead surface layers, inflammation is usually mild. WSO mostly affects toenails Occasionally, non-dermatophyte moulds such as Aspergillus terreus, or Acremonium spp.[34] has been reported. In HIV patients, SWO has been documented in fingernails as well, and is generally caused by T. rubrum.[35] The main fungus causing WSO is Trichophyton mentagrophytes.[36]

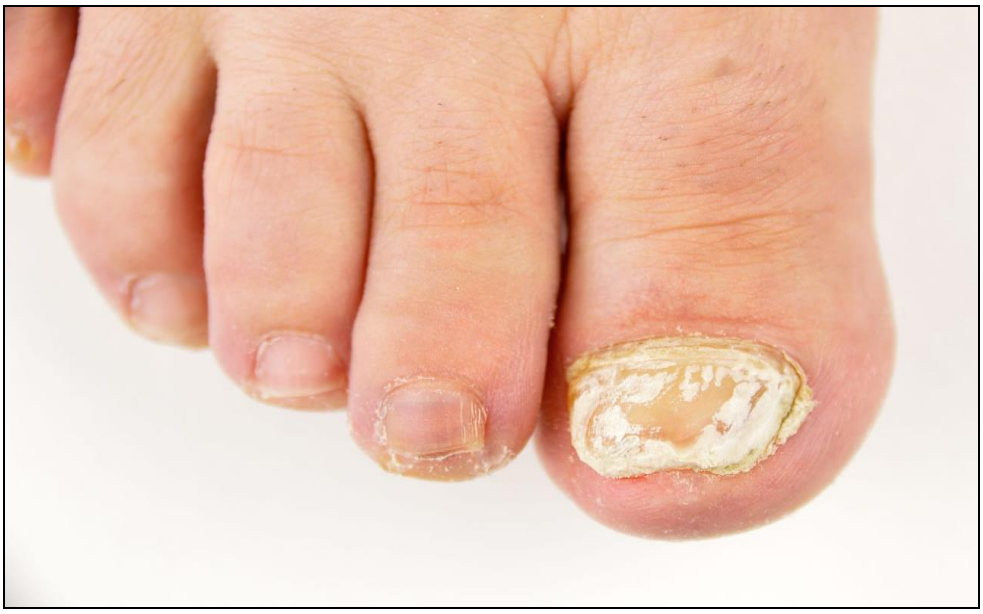

Fig. 5: White Superficial onychomycosis.

5.3 Proximal subungual onychomycosis

Proximal subungual onychomycosis((PSO) also called Proximal White Subungual Onychomycosis (PWSO) — is a rare type of nail fungus infection. It occurs when fungi enter through the proximal nail fold (near the cuticle), invade the newly formed nail plate, and then spread distally (toward the nail tip).[37]

Clinical features include: Subungual hyperkeratosis (thickened nail bed)Proximal onycholysis (nail separation near the cuticle)Leukonychia (white discoloration)Destruction of the proximal nail plate.

The main causative organism is Trichophyton rubrum. PSO spreads from the proximal nail fold and lunula area toward the distal nail, affecting all layers of the nail.[38]

Although PSO is rare in the general population, it is common among AIDS patients and is considered an early clinical sign of HIV infection.

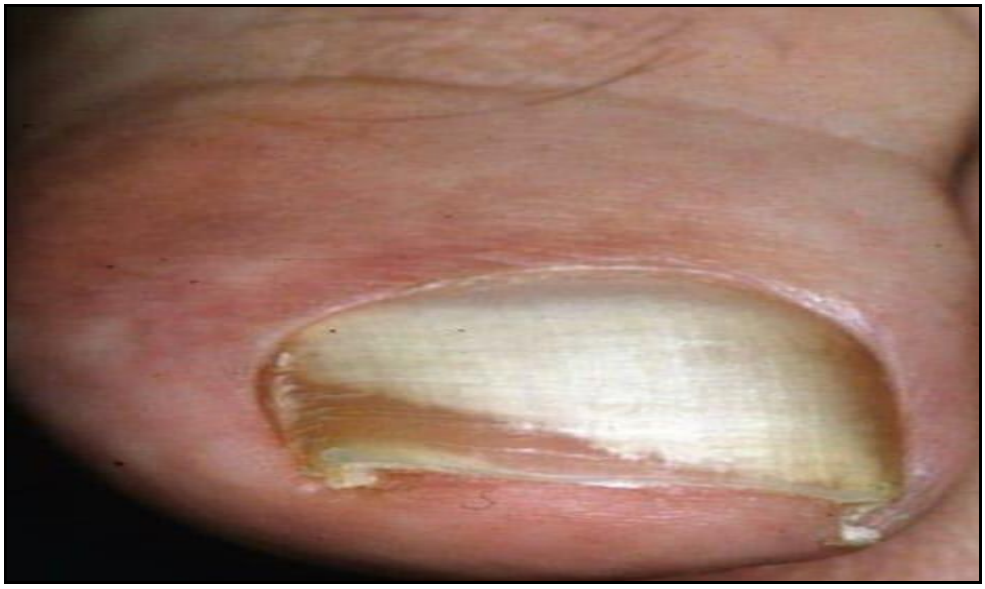

Fig. 6: Proximal subungual onychomycosis.

5.4 Total dystrophic onychomycosis

In total dystrophic onychomycosis (TDO), the entire nail is destroyed. The nail becomes brittle, breaks apart, and eventually disappears, leaving behind a thick and rough nail bed filled with hard nail material .This severe form can develop as the final stage of any other type of nail fungus. Sometimes, it appears mainly in people with chronic mucocutaneous candidiasis (CMC) or weak immune systems. In these cases, the tip of the finger becomes swollen and rounded, the nail turns thick, dull, and yellow-brown in color.[39]

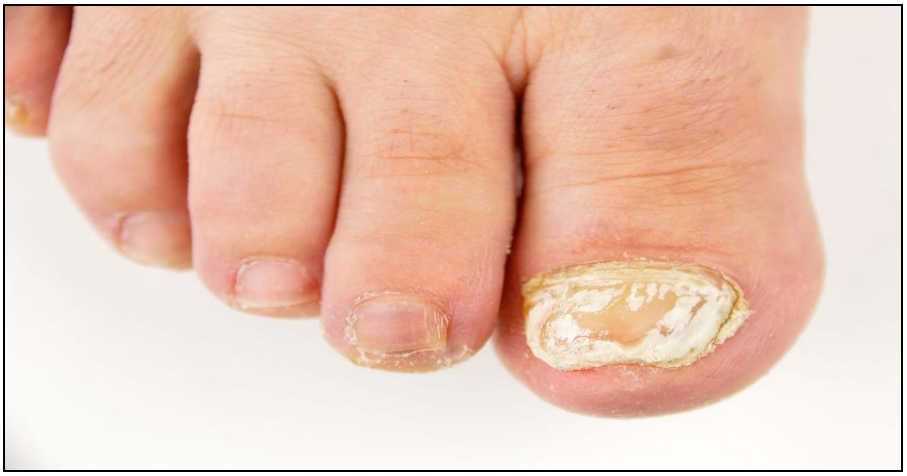

Fig. 7: Total dystrophic onychomycosis.

6. CONVENTIONAL METHOD

6.1 Direct Microscopy: This is a rapid, simple and inexpensive technique to confirm the diagnosis in a clinical setting. The collect sample is incubated in 10‑30% potassium hydroxide solution (KOH) so as to digest keratin, revealing the fungal hyphae. The easiest and quickest method for the identification of nail fungal infection is a KOH preparation.[40] The higher the percentage of KOH, the faster is the clearing. Nail specimens take a longer time to clear than skin. If there is only subungual debris or very small pieces, specimen can be examined within 10 minutes with 10‑15% KOH. However, if larger nail plate pieces are taken, they take a considerable longer time.[41] For them, the samples should be broken up into smaller parts initially itself and then incubated at 37degree Celsius for one minute and then examined. Immediately after that typical morphology of fungal hyphae can be observed under the microscope.[42]

Observation: Examine under a microscope at 400× magnification to see fungal hyphae. Improved methods: Phase contrast, dark-field microscopy, or special stains like Calcofluor white or Chicago sky blue (CSB) can improve visibility.[43]

Limitation: KOH test cannot identify the fungal species but gives a clue to the fungal group. Sensitivity ranges from 48% to 80% depending on sample quality and technique.

6.2 Fungal Culture: Another frequently used method for the diagnosis of onychomycosis is Fungal culture helps to identify the exact fungus causing the infection. It was once considered the gold standard for diagnosis but can sometimes give false results.[44] Accuracy: Sensitivity ranges from 25–80%. About 30% of tests may give false negatives, especially if the sample is too small, taken from the nail tip, or not properly crushed before testing[45] Procedure :The sample is placed on two types of media:**1.** Sabouraud's Dextrose Agar (SDA): supports growth of all fungi, including yeasts and non-dermatophyte molds (NDM) **2.** Selective medium with cycloheximide: stops the growth of common contaminants.

Cultures are kept for 3–4 weeks and checked weekly for fungal growth. Growth on both media → usually a dermatophyte .Growth only on cycloheximide-free medium → may be a non-dermatophyte mold (NDM).Sometimes, special media (like Potato Glucose Agar or Urea Agar) are used to identify the exact fungal species)[46]

NDM Diagnosis: More than one test is needed to confirm NDM infection.

The fungus is considered significant only if.

Fungal elements are also seen in the KOH test, and At least five colonies of the same mold grow, with no dermatophyte present. Because this is hard to prove, Shemer et al. suggested doing three separate cultures from different samples Fungal culture helps identify the type of fungus but takes time (weeks) and can miss infections if samples are poor.[47-48]

6.3 Histopathology

Histopathology of nail samples is useful when KOH test and culture give negative results but onychomycosis (fungal nail infection) is still suspected. It also helps to differentiate fungal nail disease from other conditions like psoriasis or lichen planus, though a nail biopsy may sometimes cause permanent nail damage.[49] A safer alternative is to send nail clippings in 10% buffered formalin for Periodic Acid-Schiff (PAS) staining. PAS stain highlights the fungal cell wall and is more sensitive than KOH or culture (about 92% vs. 80% and 59%). Other stains like Grocott Methenamine Silver (GMS) and Calcofluor White (CFW) are more specific, but histopathology cannot tell whether the fungi are alive or dead, nor can it identify the exact species. Vital stains like neutral red can show if the fungi are alive, but these can only be done on fresh samples (like scrapings or subungual debris).[50-51]

Advantages of nail clipping for histopathology

- No special fixative or transport medium needed.
- Quick processing (3–5 days)
- Shows fungal depth and invasiveness
- Painless, fast, and inexpensive compared to biopsy
- PAS-stained nail clippings give results similar to biopsy.

7. ADVANCED DIAGNOSTIC TECHNIQUES

7.1 Polymerase Chain Reaction (PCR)

PCR is a process of in vitro amplification of a DNA molecule, as a result of which within a few hours millions of copies of a particular molecule can be generated.[52] Hence, it is a very sensitive and specific method. There are different primers available to detect different species, including T. rubrum, T. interdigitale, M. gypseum, M. canis, T. tonsurans, T. violaceum, and E. floccosum. In 1999, the first special gene probe was used for the detection of T. rubrum in nail material. Because traditional tests for onychomycosis (like KOH, culture, and PAS) are not always reliable, molecular methods such as PCR have been developed.[53]

PCR testing is fast, accurate, and can identify the exact fungus directly from nail samples or fungal colonies.

Different PCR techniques include RFLP, real-time PCR, double-round PCR, and PCR sequencing. In one study of 550 nail samples, the sensitivity (ability to detect infection) was.[54]

PCR – 37% PAS – 54% KOH – 40%Culture – 22% Although PCR has very high specificity (accuracy in identifying the right fungus), it can be affected by contamination and cannot tell if the fungus is pathogenic or not. Another study by Li et al. used a triplex PCR method to detect fungi directly from nail samples.[55] Results showed: Sensitivity: PCR – 93.3%, Microscopy – 100%, Culture – 64.4% Specificity: PCR – 100%, Microscopy – 86.4%, Culture – 100% This method can also differentiate between dermatophytes, yeasts, and non-dermatophyte molds, making it a useful tool for diagnosing onychomycosis.[56]

7.2 Nail Dermoscopy (Onychoscopy)

Nail dermoscopy (onychoscopy) is a non-invasive bedside tool that allows clinicians to visualize microscopic features of abnormal nails. Key dermoscopic features of distal and lateral subungual onychomycosis include a jagged proximal edge of the onycholytic area with spikes and longitudinal striae. These features and a ruins aspect are associated with total dystrophic onychomycosis.[57] Homogenous opacity is found in superficial onychomycosis. Onychomycosis can also present with longitudinal melanonychia (fungal melanonychia). In such cases, white or yellow streaks, non-longitudinal homogenous pattern, yellow coloration, reverse triangular pattern, subungual hyperkeratosis, multicolor pattern and nail scaling are positive predictors of fungal melanonychia (Figures 1G,H) compared to nail matrix naevi or subungual melanomas.[58] As nail dermoscopy is quick, non-invasive and inexpensive, it has the potential to help physicians identify onychomycosis by the bedside and decide whether to proceed to mycological assessment.[59]

7.3 Optical Coherence Tomography

It allows for non invasive and noncontact cross‐sectional imaging of biological tissue by detecting backscattering near infrared light of the in homogenities within the sample. The longitudinal and transverse tomograms in OM show a thickening of the nail plate within which signal intense structures surrounded by low scattering areas are visible. If histologically correlated, the high‐scattering structures are conglomerates of hyphae which

reflect more light due to their high chitin concentration and hence appear with higher signal intensity. The low scattering areas represent the surrounding lacunae of the hyperkeratotic nail plate. The results of OCT are comparable to the findings of PAS stained specimen and have been found to be superior to KOH preparations and cultures. Thus, OCT is a reliable, easy to use, non invasive and non destructive method to visualize fungal elements in vivo, even in cases with false negative KOH‑preparation and culture. Furthermore, it offers the opportunity to screen several areas within a nail plate and hence detect persisting fungal elements during local or systemic therapy.[60] However, larger studies are required to confirm the utility of this procedure. Also, its availability and cost effectiveness are not favourable for use in clinical practice.

8. TREATMENT STRATEGIES

Treatment for toenail fungus isn't always needed. And sometimes self-care and nonprescription products clear up the infection. Talk with your health care provider if your condition doesn't improve. Treatment depends on the severity of your condition and the type of fungus causing it. It can take months to see results. And even if your nail condition improves, repeat infections are common.

Medications Your health care provider may prescribe antifungal drugs that you take by mouth (orally) or apply to the nail.

8.1 Topical Antifungal

Topical antifungal therapy is used only in superficial onychomycosis, which affects up to one-third of the nail plate. The most commonly used medications are Ciclopirox (Poli nail nail lacquer, Batrafen nail lacquer), Efinaconazole (Exoderil solution), and others. An antifungal nail lacquer can be used in onychomycosis which affect up to 40 % of the nail surface or not more than three out of ten nails. According to the international consensus conference of onychomycosis the fungal affection should not exceed 50 % of the nail surface However, some nail lacquers are approved for treatment of an onychomycosis up to 80 % of the nail surface .Common Topical Antifungal Agents.[61]

Ciclopirox: - A broad-spectrum antifungal medication called ciclopirox is sold as nail lacquer. It kills a wide range of microorganisms, including Gram-positive and -negative bacteria, dermatophytes, candida, and even some non dermatophytic fungus. To treat mild to severe onychomycosis caused by Trichophyton rubrum in immunocompetent patients who do

not have lunula involvement, the FDA approved a nail polish containing 8% ciclopirox in 1999. Only local responses like burning or periungual erythema were reported.[62]

Efinaconazole:- A newer and effective topical antifungal medication is fluconazole. In clinical studies, this once-daily topical solution has been demonstrated to be more effective than previous therapies. Usually used for 48 weeks, fluconazole is administered directly to the afflicted nail. It works very well against dermatophytes, which are the most frequent cause of onychomycosis. Clinical trials show cure rates between 10% and 20%, with mild-to-moderate patients showing better results.[63]

8.2 Systemic therapy

Systemic therapy: Onychomycosis is typically treated with systemic drugs Because to their wide availability, low cost, and great Efficacy. The FDA has approved terbinafine, Griseofulvin, and itraconazole to treat onychomycosis, And oral fluconazole is also administered off-label.[64]

a. Terbinafine

Terbinafine is an allylamine that inhibits the activity Squalene epoxidase; this property makes it highly Effective against dermatophytes but less so against non dermatophytic moulds and Candida spp. The Food and Drug Administration (FDA) approves oral Administration of 250 milli grammes (mg) once day for 6 weeks for treating onychomycosis caused by Dermatophytes on fingernails and 12 weeks for treating Onychomycosis caused by fungi on toenails (2)Headache, stomach issues, and skin rashes are the most Often reported adverse reactions. Occasionally, you can Experience some changes in your liver enzyme levels or Your sense of taste. Reactions.[65]

Terbinafine pulse dosing: Despite not being approved by the FDA, pulse-dose Therapy with terbinafine can be used to treat Onychomycosis. The most efficacious of the pulse Regimes was a 3-cycle course of 250 mg/day for 4 weeks On and 4 weeks off; mycologic and complete cure rates Were comparable to those reported with continuous 250 Mg/day terbinafine treatment for 12 week.[66]

b. Fluconazole

Inhibiting lanosterol 14-demethylase, like another Triazole, makes it effective against dermatophytes, Candida species, and some non-disseminated fungi. Unlike itraconazole,

fluconazole is absorbed well Regardless of stomach acidity or whether or not food has Been consumed. Treatment for onychomycosis requires 150 mg once weekly until the entire nail grows out (6-9 Months for fingernails, 12-18 months for toenails). The Small amount still present in the nails requires a Prolonged treatment schedule. The most common side Effects include headache, nausea, rash, stomach pain, And elevated transaminases. Liver damage is a rare Complication, and occurs mostly in people who are Immunocompromised. Fluconazole inhibits the Enzymes CYP2C9 and CYP3A4 to varying degrees, Necessitating care when used in conjunction with other Drugs.[67]

8.3 Combination Therapy

Combining different treatment options for onychomycosis can often improve results by using drugs with different actions, reducing the chance of fungal resistance, and enhancing drug effectiveness. Studies have shown that using both oral and topical antifungal agents together can sometimes be more effective than using one treatment alone. Common combinations include oral terbinafine or itraconazole with topical agents such as amorolfine, ciclopirox, or terbinafine creams or lacquers.[68]

Although oral antifungal medicines are effective, complete cure is often difficult to achieve. In most studies, the fungal (mycological) cure rate is about 30% higher than the visible (clinical) cure rate, and at least 25% of patients do not respond fully to treatment.[69] To improve results and reduce relapse, combination therapy — using both oral and topical treatments — is often used. Oral medicines reach the nail bed but may not penetrate the outer or side parts of the nail well, while topical medicines can reach the nail surface and edges but not the deeper layers. By combining both types, better drug coverage is achieved. Oral drugs build up slowly but stay in the nail for a long time, while topical agents like amorolfine start acting within hours. Using both together can also allow lower oral doses, improving tolerance and reducing side effects. Studies show that: Using itraconazole + amorolfine lacquer achieved an 83% cure rate, compared to 41% with itraconazole alone. Terbinafine + amorolfine lacquer showed a 27% cure rate, compared to 17% with terbinafine alone.[70] Combination with nail debridement or surgery can further help by reducing fungal load and improving drug penetration. Combination therapy can be used in two ways: Parallel: Oral and topical drugs are given together Sequential: Oral drug is given first, followed by topical therapy.[71]

8.4 Surgical Theraphy

It is considered that onychomycosys is one of the fungal infections among population with the highest percentage of unsuccessful treatment. Although rarely used independently, surgical treatment is an alternative to systemic therapy.[72] Topical antifungal medications are used at the same time and/or immediately after that, aiming at elimination of the infected nail structures. Surgical treatment could be accompanied by topical or systemic therapy. Surgical nail plate removal could be combined with topical antifungal therapy. This method provides very good clinical results. Such treatment has been applied in cases of Scopulariopsis brevicaulis and Acremonium species infections. Surgical treatment is also necessary in fungal infections resistant to systemic or topical treatment. Besides avulsion (the forcible tearing away of nail plate), the mechanical therapy of onychomycosis includes abrasion (scraping off the superficial layer) of the nail.[73] Partial avulsion is recommended in cases of distal lateral subungual onychomycosis and partial subungual onychomycosis as an adjuvant to local therapy.

8.5 Photodynamic Light Therapy

Photodynamic therapy (PDT) is a non-invasive treatment method that uses a combination of a photosensitizing agent and light of a specific wavelength. The interaction between these components produces singlet oxygen, a reactive molecule that destroys fungal cells.[74] PDT has been evaluated for its potential to treat superficial nail infections, including those caused by molds such as Acremonium sclerotigenum.In one clinical protocol, PDT combined with methyl aminolevulinate (MAL) is applied in three treatment sessions spaced 15 days apart. Another approach utilizes 5-aminolevulinic acid (ALA) as the photosensitizer.[75] The dermatophyte Trichophyton rubrum, a major cause of onychomycosis, converts ALA into protoporphyrin IX (PpIX), which fluoresces red under Wood's lamp or fluorescence microscopy. ALA concentrations between 1 and 10 mmol/L have been found optimal for antifungal activity, while higher doses may inhibit PpIX formation. When ALA is combined with light exposure, a clear inhibitory effect on fungal growth is observed, making PDT a promising strategy to reduce T. rubrum colonization.[76] A commonly used PDT regimen involves first softening the nail by applying 20% urea ointment under occlusion for about 10 hours. Then, a 20% solution of ALA methyl ester is applied to the nail and covered with light-protective material for approximately 5 hours. The presence of PpIX is confirmed using ultraviolet light or a spectrophotometer. Laser irradiation (typically at 630 nm, 100 J/cm²) is then delivered to the nail surface. Treatments are performed weekly, and improvement is

usually observed after 6–7 sessions (total dose 600–700 J/cm²). Some mild discomfort may occur during the procedure but typically resolves within a day.[77]

Post-treatment evaluations often show negative fungal cultures and KOH microscopy, and relapses are rarely seen within 3–6 months of follow-up. PDT with ALA or methyl aminolevulinate has also demonstrated success in treating cases of onychomycosis caused by nondermatophyte molds and T. rubrum in distal and lateral subungual forms.[78]

9. PROGNOSIS

The relapse rate of onychomycosis is 20% to 25%, with the condition likely to recur within two years of successful therapy.[79] Features associated with poor prognosis include age older than 70 years, history of nail trauma, and diabetes.[80]

10. CHALLENGE IN MANAGEMENT OF TREATED PATIENT

Onychomycosis is notoriously difficult to treat. Achieving complete cure can take as long as 18 months and cure is not achieved at all in 20–25% of treated patients. Furthermore, the disease is associated with very high recurrence rates due to the presence of residual fungal spores or hyphae, with relapse occurring in 6.5–53% of patients. The efficacy of current treatments is limited by the slow growth of toenails, nail keratin thickness preventing penetration of topical and systemic drugs, and survival of fungi in surrounding environments (such as footwear) for long periods.[81] Because of their lack of intrinsic immune function and impenetrable nature, nails are a particularly challenging tissue to cure. Individuals with onychomycosis can experience very long-lasting disease, especially in the absence of effective treatment. An average disease duration of almost 18 years was recorded among 2761 onychomycosis patients in Poland.[82] Susceptibility to onychomycosis increases with the presence of other underlying comorbidities, including chronic renal failure (with dialysis) and renal transplant, immunodeficiency, diabetes, cancer and peripheral arterial disease. Although low, the possibility exists of hepatic injury during therapy with the newer antifungal agents, and it should remain consideration. Liver function tests at baseline and periodically during therapy should be performed for patients receiving continuous therapy with terbinafine, fluconazole, or itraconazole.[83] Patients receiving terbinafine are also advised to undergo baseline and periodic complete blood counts as well. Pulse therapy with itraconazole does not require laboratory monitoring. The recommendations for intermittent therapy with fluconazole are unknown. In all cases, patients should be educated so that they

can recognize and report signs of drug related adverse reactions, including jaundice, upper abdominal tenderness, malaise, dark urine, pale stools, fatigue, nausea, and vomiting.[84]

11. PREVENTION OF ONYCHOMYCOSIS

Prevention of Onychomycosis (fungal infection of the nail) can be prevented by adopting proper hygiene practices, minimizing exposure to fungi, and maintaining good nail health.[85]

11.1 Personal Hygiene

Keep feet clean and dry, especially between the toes.

Wash feet daily with soap and water, and dry them thoroughly.

Change socks daily and wear breathable footwear to reduce moisture buildup.

Use antifungal foot powders or sprays if prone to excessive sweating.

11.2 Nail Care

Trim nails straight across and keep them short.

Avoid nail trauma—injuries can allow fungi to enter the nail bed.

Do not share nail clippers, files, or footwear with others.

Disinfect nail tools regularly (e.g., with 70% alcohol).

11.3 Footwear and Environment

Wear shoes or sandals in public places such as pools, gyms, and locker rooms.

Prefer cotton socks and well-ventilated shoes.

Rotate shoes to allow them to dry completely between uses.

11.4 Medical and Lifestyle Measures

Treat tinea pedis (athlete's foot) promptly to prevent spread to nails. Maintain proper blood glucose control in diabetic individua Avoid unnecessary or prolonged use of occlusive footwear. People with immunosuppression should take extra precautions and seek early treatment for any signs of fungal infection.

12. CONCLUSION

Onychomycosis is a common and often persistent fungal infection that affects both fingernails and toenails, leading to discoloration, thickening, and nail deformity. Although it may seem like a minor cosmetic issue, it can cause significant discomfort, pain, and psychological distress—especially in the elderly and individuals with diabetes or immunosuppression. Early diagnosis through microscopy, culture, histopathology, or

advanced molecular techniques like PCR is essential for effective management. Treatment includes topical, systemic, and combination antifungal therapies, as well as newer approaches such as laser and photodynamic therapy. However, due to the chronic nature and high relapse rate of the infection, prevention remains the most effective strategy. Maintaining good foot and nail hygiene, avoiding trauma and moisture, promptly treating athlete's foot, and adopting preventive lifestyle habits can greatly reduce the risk of infection and recurrence. With proper awareness, early intervention, and adherence to treatment and preventive measures, the overall prognosis of onychomycosis can be significantly improved.

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