

Onychomycosis as a Cause of Onychodystrophy: A Narrative Review

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ABSTRACT

Onychodystrophy is defined as the disruption of the nail plate and can be caused by a number of infective and noninfective causes. Often, the treatment modalities and the prognostic outcomes differ according to the underlying etiology of nail dystrophy. Hence, an understanding of the anatomy of the nail unit and clinical presentations of various acquired causes of onychodystrophy is necessary to address the underlying cause and treat accordingly.

Keywords: Nail, Nail dystrophy, Onychodystrophy.

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INTRODUCTION

Nails, in spite of being a small portion of the human anatomy, play a significant role as a window for systemic diseases and have received major attention as an aesthetic component. The term "onyx" is derived from the Greek word *ónux* meaning nail.¹

Onychodystrophy is a broad term and is often used to describe the discoloration or disruption or brittleness of the nail plate. Most authors describe it as the partial or complete disruption of the nail plate caused by various endogenous or exogenous factors.^{2,3}

There are several underlying etiologies for onychodystrophy, such as fungal and nonfungal infections, noninfectious inflammatory conditions, systemic diseases, trauma, drugs, and rarely tumors.⁴ Studies show that trauma, onychomycosis, and nail psoriasis are the most common causes of onychodystrophy. Drugs like systemic antibiotics, antineoplastic drugs, and antiretroviral drugs are implicated in the disruption of the nail plate.

It is essential that the specific cause of onychodystrophy be identified so that adverse effects and the cost of empirical therapy, such as systemic antifungals, are avoided.

The various acquired causes of nail dystrophy are discussed in this article. The necessary literature search was done with the help of databases like Google Scholar and PubMed using keywords such as "nail dystrophy," "nail disorders," "nail infections," and so on, and 50 relevant articles published between 2001 and 2020 were recruited.

THE NAIL UNIT

Embryology of the Nail

Nail development begins by the 8th week and is completed by the 20th week of gestation. It begins as a condensation of the epithelial cells on the dorsal aspect of the distal phalanx called the apical ectodermal ridge and develops into the placode.² At 10 weeks, the future nail bed appears as an ovoid continuous shallow groove formed by the invagination of the placode, and extends beyond the tip of the finger. Later, the proximal, distal, and lateral nail grooves develop and the nail becomes flat. The nail field grows proximally, and the nail plate emerges from the proximal nail fold by week 14. Keratinization occurs in a distal to proximal direction.³ The nail bed is covered by the nail plate by the 5th month of gestation. The cells

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of the nail bed gradually cease producing keratohyaline granules and become parakeratotic. After 22 weeks, the distal groove disappears and the nail plate overgrows the tip of the digits and continues to grow throughout life.

Anatomy of the Nail Unit

Nails occupy approximately one-fifth of the dorsa of the digits and 30% of the great toes. The nail apparatus constitutes the following:

- Nail plate
- Nail matrix
- Nail bed
- Nail folds
- Cuticle
- Lunula

Nail plate: It is a rectangular translucent plate made up of hard keratin and composed of well-differentiated keratinocytes called onychocytes.⁴ The thickness of the nail plate varies from 0.5 to 0.75 mm and is usually convex both longitudinally and transversely. Each nail plate comprises a thin dorsal lamina, a thick intermediate layer, and a ventral layer histologically. Onychocytes are flatter and they do not desquamate periodically.

Nail matrix: The nail matrix, which is the germinative portion of the nail unit, is divided into the proximal and the distal matrix. An opaque crescentic structure can be seen as the distal end of the matrix passes the proximal nail fold and is called the lunula.

The nail plate is formed from the nail matrix by a process called “onychokeratinization” or “matrical keratinization.”⁵ Unlike normal skin, the nail matrix contains melanocytes in the basal and the suprabasal layers but they are unable to produce melanin.

Nail bed: The nail bed is the soft tissue on which the nail rests. It contains blood vessels, lymphatics, elastic fibers, and fat cells. There is no subcutaneous adipose tissue, melanocytes, or appendages in the nail bed.

Nail fold: There are proximal and two lateral nail folds. The proximal nail fold is the continuation of the digital epidermis but is devoid of dermatoglyphic markings and pilosebaceous glands. The distal ventral surface of the proximal fold forms the eponychium, which continues as a thick layer of stratum corneum that extends over the nail plate called the cuticle. The lateral nail folds protect the sides of the nails.

Vascular, nerve, and lymphatic supply: The nail bed is richly supplied by anastomoses from the branches of the digital arteries. Neurovascular bodies called glomus bodies are present in the nail bed, and they represent arteriovenous anastomoses without intervening capillaries. The blood drains into the larger veins into the subcutaneous layer of the dorsal and the volar aspect of the digits. The perionychial part is supplied by the dorsal branches of the paired digital nerves. The nail bed has numerous lymphatic vessels, especially near the free edge of the nail.

Fingernails grow at a rate of approximately 3 mm per month and toenails around 1 mm per month. Factors like low temperature, female gender, nondominant hand, first and fifth digits, certain disease states, and medications lead to a slower growth rate.⁴

Nail Disorders

A detailed list of various nail disorders are mentioned below:

Abnormalities in the Shape of the Nail Plate

- Brachyonychia—width of the nail is disproportionately greater than the length
- Dolichonychia—the length of the nail is disproportionately greater than the width
- Clubbing—an increase in the transverse and longitudinal curvature of the nail along with soft tissue hypertrophy of the nail bed
- Koilonychia—spooning of the nails caused by a reversal in the curvature of the transverse and longitudinal axes of the nails
- Pincer nails—increase in the transverse curvature of the nails along their longitudinal axis with the greatest proportion at the tip
- Micro and macronychia—the nail is very small or large compared to the other nails

Abnormalities in Nail Attachment

- Pterygium—proximal nail fold fuses with the nail matrix and the nail bed
- Inverse pterygium—hyponychium attaches to the nail plate thus obliterating the distal nail groove
- Onycholysis—distal detachment of the nail plate from the nail bed
- Onychomadesis—proximal detachment of the nail plate from the nail bed

Abnormalities of the Nail Plate Surface

- Onychorrhexis—longitudinal grooving or ridging in the nail plate
- Onychodystrophy—partial or complete disruption of the nail plate associated with thickening, discoloration, roughening, and splitting
- Beau’s lines—horizontal grooves in the nail plate
- Pitting—punctate depressions on the nail plate caused by parakeratotic cells in the nail plate
- Onychoschizia—transverse and lamellar splitting of the distal portion of the nail plate

Abnormalities of Nail Color

Some abnormalities of nail color are given here.⁶⁻⁸

- Leukonychia—whitish discoloration of the nail
- Mees’ lines—one or more white transverse lines that do not disappear on blanching
- Muehrcke’s lines—two white transverse lines parallel to each other
- Half and half/Lindsay nail—normal proximal half and brownish discolored distal half
- Terry’s nails—normal distal half and white proximal half
- Melanonychia—longitudinal or transverse, brownish or blackish pigmentation of the nails
- Cyanosis—bluish discoloration of the nails as a result of an increase in deoxygenated blood
- Splinter hemorrhages—extravasation of blood from the blood vessels of the nail bed
- Red lunula—erythema of the lunula prominent over the thumb
- Yellow nail syndrome—thickening and yellowish green discoloration of the nails

Onychodystrophy associated with Old Age

Nail disorders are commonly seen in the elderly age group due to various factors like UV radiation, trauma, impaired peripheral circulation, physiological alterations in the nails, infections, systemic or dermatological diseases, drugs, and so on. With advancing age, there is an increase in the calcium content of the nails and size of the keratinocytes. Moreover, the average growth of the nail decreases and the average turnover rate is altered in older age leading to a thickened nail plate and onychorrhexis, respectively. Water content of the nails decrease with age leading to brittle and easily breakable nails in old age.⁹

Traumatic onychodystrophy is common in the older age group. It is characterized by nail plate thickening, pincer nails, onychogryphosis, traumatic splinter hemorrhage, subungual hematoma, subungual hyperkeratosis, and subungual callus.

Onychomycosis is the commonest nail infection occurring in almost 20% of the people over 60 years of age. Acute or chronic paronychia, which is the infection and inflammation of the nail folds caused by *Candida* and other Gram-negative bacteria are also common in old age.

Various systemic diseases like diabetes mellitus, hypertension, chronic kidney disease, liver diseases, and pulmonary diseases are also associated with nail changes. Chronic inflammatory skin conditions like psoriasis, eczema, and erythroderma are also present with nail changes in the elderly.

According to a study done on elderly white population, subungual melanoma of the great toe was common with the peak

incidence in the eighth decade. Other neoplasms which were reported to be common in old age are Bowen's disease, squamous cell carcinoma, basal cell carcinoma, and glomus tumor.

In a study conducted in 100 patients over 60 years, by Rao et al. in Kolkata, India, the following nail changes were seen. Prominent longitudinal ridges were the commonest (85%), followed by rough nails in 33%, transverse ridges in 23%, and lamellar split in 15% of cases; 40% of the males and 26% of the females included in the study had brittle nails. Onychauxis or thickening of the nail plate was noticed in 23% of the participants. Among the infective conditions, onychomycosis was seen in 16%, followed by chronic paronychia in 9%. Psoriatic nail changes were seen in 67% of the patients.¹⁰

Nail Disorders associated with Systemic Diseases

Nails serve as an important diagnostic tool in the identification of various systemic diseases. Fingernail changes are more specific than toenail changes because toenails are frequently subjected to trauma. Nail changes can be associated with pulmonary, cardiac, gastrointestinal, renal, endocrine, autoimmune, infectious, nervous system, and psychological diseases. Nail changes such as Mees' lines, Muehrcke's lines, Terry's nails, half-and-half nails, and clubbing are more specific nail changes associated with systemic diseases (Table 1).

Common nail changes associated with systemic diseases have been evaluated in several previous studies.¹¹⁻¹⁸

Nail Changes associated with Dermatological Diseases

Nail changes that can be associated with dermatological diseases are listed in Table 2.

ONYCHOMYCOSIS

The term "onychomycosis" is derived from two Greek words: *onychos* meaning nail and *mycosis* meaning fungal infection.²² Therefore, fungal infection of the nails is called onychomycosis. It can be caused by dermatophytes or nondermatophytic molds and yeasts. It is referred to as tinea unguium when the causative agent is a dermatophyte. The incidence of onychomycosis is reported to be 0.5-5% in various studies conducted among the Indian population. Though various studies have concluded that dermatophytes are the common etiologic agents causing onychomycosis,²³ nondermatophytic molds and yeasts are commonly implicated in causing onychomycosis in previously traumatized nails.^{22,24} Hence, it is important to identify and isolate the organism for successful treatment and to prevent recurrence.

Table 1: Common nail changes associated with systemic diseases

Koilonychia	Melanonychia
Clubbing	Splinter hemorrhages
Pincer nail	Yellow nail syndrome
Dolichonychia	Red lunula
Brachyonychia	Nail bed telangiectasia
Onycholysis	Pterygium
Onychorrhexis ¹⁹	Onychoschizia
Mees' lines	Beaus lines
Muehrcke's lines	Onychocryptosis
Half-and-half/Lindsay nails	Onychogryphosis ²¹
Terry's nails ²⁰	

Table 2: Common nail changes associated with dermatological diseases

<i>Nail changes</i>	<i>Dermatological conditions</i>
Trachyonychia	Lichen planus, psoriasis, alopecia areata, ¹⁴ atopic dermatitis, ichthyosis vulgaris, incontinentia pigmenti ¹⁵
Onycholysis	Psoriasis, onychomycosis, ACD ¹⁶
Subungual hyperkeratosis	Psoriasis, ACD
Beau's lines	Psoriasis, pemphigus
Pitting	Psoriasis, alopecia, eczema, lichen planus ¹⁷
Oil drop sign/Salmon patch	Psoriasis ¹⁸
Pincer nail	Psoriasis, onychomycosis ¹⁹
Splinter hemorrhages	Psoriasis, SLE, Scleroderma
Red lunula	SLE
Pterygium	Lichen planus
Pterygium inversum	Scleroderma ²⁰
Longitudinal melanonychia	Trauma, nail matrix nevus, melanoma
Yellow chromonychia	Psoriasis, onychomycosis, alopecia areata
Green chromonychia	<i>Pseudomonas aeruginosa</i> infection ²¹

ACD, allergic contact dermatitis; SLE, systemic lupus erythematosus

Epidemiology

The prevalence of onychomycosis is estimated to be 5.5% (2-8%) according to various studies conducted worldwide. However, the prevalence rate in India stands between 52 and 72% owing to the hot and humid climate prevailing.²⁵ A study conducted by Cozzani et al. in 2012 in Italy in 100 elderly patients with onychodystrophy, the prevalence of onychomycosis was found to be 36%.²⁶ Various factors like old age, systemic diseases especially diabetes, chronic inflammatory skin conditions like psoriasis, immunosuppression, obesity, smoking, occupation, trauma, and ill-fitting shoes are commonly implicated as the predisposing factors for onychomycosis. It is less common in children because of the faster nail growth rate and lesser susceptibility to wear and tear. Dermatophytes account for 90% as the causative agent for onychomycosis whereas nondermatophytic molds have a prevalence rate of 1.45-17.6%.²⁴ The common dermatophytes causing onychomycosis are *Trichophyton rubrum*, *Trichophyton mentagrophytes* var. *interdigitale*, and *Epidermophyton floccosum*.²⁷ The nondermatophytic molds attributable to cause onychomycosis are *Aspergillus* sp, *Scopulariopsis brevicaulis*, *Cladosporium Acremonium* sp, *Paecilomyces* sp, *Tritirachium oryzae*, *Fusarium* sp, *Phialophora* sp, *Rhizopus* sp, and *Alternaria alternata*.^{22,28} Onychomycosis can be divided into the following five types:

- Distal lateral subungual onychomycosis (DLSO)—62.5%
- White superficial onychomycosis (WSO)
- Proximal subungual onychomycosis (PSO)
- Endonyx onychomycosis (EO)
- Mixed pattern onychomycosis (MPO)
- Total dystrophic onychomycosis (TDO)—37.5%^{22,27}

In a study conducted by Sarma et al. in 302 suspected cases of onychomycosis in North India, they found that the commonest type

of onychomycosis caused by dermatophytes was DLSO type (62%) followed by total dystrophic onychomycosis (20.2%).²⁹

Common Predisposing Factors

A few common predisposing factors of onychomycosis are discussed here.

Age and sex: The prevalence of onychomycosis is found to be greater than 40% in individuals older than 60 years in various studies. In a study conducted by Kumar et al. in Rajasthan, onychomycosis was common in the middle age group (31–40 years) due to their work.³⁰ In various studies conducted in India and other countries, onychomycosis was more common in men than in women.³¹

Occupation: Onychomycosis is associated with occupations involving constant trauma and wet work. This could be explained by increased trauma which facilitates easy entry of the organisms into the nails. Prevalence of onychomycosis was found to be 43.3% among patients who did wet work and 26.6% among housewives.³¹ Abasti et al. reported a higher frequency of onychomycosis caused by nondermatophytic molds in housewives.²² Among the housewives, finger nails were commonly involved.

Other factors: Onychomycosis was a common finding in diabetic patients.^{32,33} This is because of poor circulation, impaired wound healing, and decreased sensory neuropathy associated with diabetes.²⁵ In diabetics, onychomycosis caused by dermatophytes is more common than that caused by *Candida* and nondermatophytic molds.³⁴ A study conducted by Baiu et al. in Libya, the prevalence of onychomycosis among diabetic patients was 77.2%.³⁵ In a study conducted by Sarma et al. in North India, 3.9% of the patients were diabetics.²⁹ Toenail onychomycosis, especially the proximal subungual type, is common with immunosuppressed patients like HIV patients and posttransplant and dialysis patients. Other predisposing factors are peripheral vascular disease, trauma, and immunosuppression.³⁶ Recurrence can be precipitated by genetic predisposition, trauma, and inappropriate treatment.³⁷

Associated dermatological conditions: Psoriasis is a predisposing factor as it can result in nail plate detachment, allowing fungal colonization of the nail bed. Studies have shown the prevalence of onychomycosis to be 13–47% in psoriasis patients. In a study conducted by Chaowattanapanit et al., in psoriatic nails, the most commonly isolated fungi was *Candida* spp. (41.9%) and toenails were nondermatophytic molds.³⁸ In another study conducted by Romaszkievicz et al. in Poland, the prevalence of onychomycosis in patients with psoriasis was 23.53% and molds were the commonest organisms isolated.³⁹ It is also commonly associated with other dermatophyte infections like tinea corporis, tinea pedis, and tinea manuum. In a study conducted by Reddy et al. in Kadapa, India, onychomycosis is also associated with other conditions like hyperhidrosis, paronychia, lichen simplex chronicus, eczema, and fissure foot.³¹

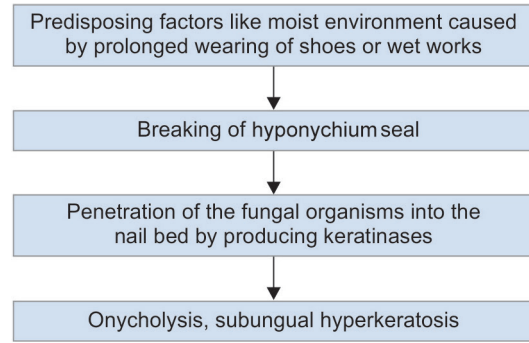
Pathophysiology

Flowchart 1 explains the pathophysiology of onychomycosis.⁴⁰

Clinical Features

Onychomycosis of the toenails is more common than the finger nails as the growth rate of toenails is three times lesser than that of the finger nails. In a study conducted by Gupta et al. in

Flowchart 1: Pathophysiology of onychomycosis



130 patients in Himachal Pradesh, India, toenails (56.9%) were involved more than finger nails (32.3%).⁴¹ It is characterized by onycholysis, leukonychia, subungual hyperkeratosis, periungual inflammation, destruction of nail plate, and pitting.^{23,42} The duration of the lesion in most cases is less than one year. Isolated onychomycosis was usually associated with nondermatophytic molds (Flowchart 1). Few patients with onychomycosis caused by *Aspergillus niger* presented with a blackish discoloration of the lunula.⁴² Other features associated with onychomycosis caused by *Aspergillus* species were thickened nails (93%), brittle nails (89%), and discolored nails (85%).⁴³

Diagnosis

The clinical picture of onychomycosis caused by different organisms are sometimes indistinguishable from each other. Hence, it is important to isolate the organism for proper and adequate treatment. Various methods used in the diagnosis of onychomycosis are

- KOH mount,
- Fungal culture,
- Histopathology,
- Dermoscopy, and
- DNA-based techniques.

KOH mount and culture are the time-tested methods of diagnosing onychomycosis. Though culture is considered as the gold standard technique in diagnosing onychomycosis, histopathology is done to diagnose and differentiate it from other inflammatory dermatological conditions like lichen planus and psoriasis. Other rarely used techniques are polymerase chain reaction, confocal laser microscopy, phase contrast microscopy, Vitek, and matrix-assisted laser desorption/ionization time of-flight (MALDI-TOF) mass spectrometry.⁴⁴ In a study conducted by Shenoy et al. in 101 patients with clinically diagnosed onychomycosis, to compare the standard mycological tests with histopathology, 35% showed positive culture out of which 63% were nondermatophytic molds, out of which *Aspergillus* was the most common isolate.⁴⁵

Although the culture has high specificity, it is time consuming and requires an appropriate medium, temperature conditions, and the existence of viable fungus. Contamination by bacteria and other opportunistic fungi may compromise the correct diagnosis. Currently, the diagnostic gold standard is the association of direct mycological test with culture. However, this results in a minimum of 30% false negatives and shows sensitivity varying from 25 to 80%.⁴⁶

Treatment

Onychomycosis is more often considered a cosmetic problem by the patient. However, it is a difficult-to-treat situation and often takes months together to achieve cure. The desired endpoints are described in terms of mycological, clinical, and complete cure. Mycological cure is defined as negative KOH and microscopy and fungal culture. Clinical cure is defined as a nail with absent clinical signs of onychomycosis whereas complete cure is defined as a nail having both mycological and clinical cure. Treatment modalities can be topical, systemic, or both.

Topical antifungals commonly used are:

- Ciclopirox 8%,
- Amorolfine 5% lacquers, and
- Efinaconazole 10% solution⁴⁷

Systemic antifungals that are commonly used to treat onychomycosis are given below:

- Azoles — fluconazole, itraconazole
- Allylamines—terbinafine
- Griseofulvin

Other modalities to treat onychomycosis are as follows:

- Combination therapy—systemic and topical
- Sequential therapy which uses both azoles and allylamines
- Boosted oral/topical antifungal treatment
- Surgical debridement and avulsion
- LASER therapy⁴⁸

ACUTE AND CHRONIC PARONYCHIA

Infection of the nail folds is called paronychia. It occurs due to the disruption of the proximal nail fold seal thereby allowing penetration of microorganisms into the nail tissue. It is acute if the duration is less than or equal to 6 weeks and chronic if it is more than 6 weeks. Prolonged exposure to moisture is an associated risk factor. *Staphylococcus aureus*, *Streptococci* and *Pseudomonas* are the common microorganisms implicated as causative agents of paronychia.⁴⁹ It can also be caused by Gram-negative organisms, herpes simplex virus, dermatophytes, and yeasts like *Candida*. It commonly presents as erythematous tender swelling of the nail folds sometimes associated with an abscess formation. Systemic antibiotics along with abscess drainage when present are the main modalities of treatment.

CONCLUSION

Nail disorders closely mimic each other, and it is essential to differentiate them for a better prognostic outcome. As onychomycosis presenting as onychodystrophy is difficult to be identified clinically, it can be diagnosed with the help of microbiological or histopathological techniques so that patients with onychomycosis can be treated with antifungals and empirical use of antifungals in onychodystrophy due to other causes can be avoided thereby preventing its adverse effects and antifungal resistance.

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