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Onychomycosis: Pathogenesis, Diagnosis, and Management. An over view

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Contents

Abstract:

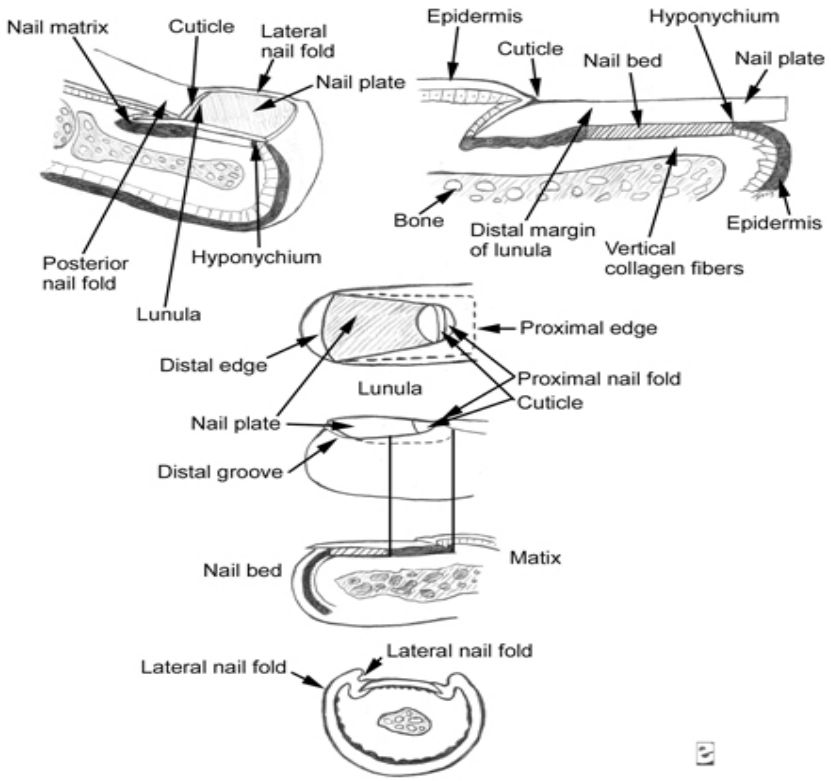
Onychomycosis is the common fungal infection which has apparently sanction to many causes of starting point occurrences e.g. discoloration, splitting of the nail from the nail bed. Candida species, dermatophytes, non-dermatophyte with certain other examples are the type of species, along with the possession of varying percentage at different levels, to have an influence on particular disease's consequences. According to the optimum condition provided for onychomycosis culture to grow on an increase or decrease its growth by assistance to it with changing temperature. Under certain observation, its limitation has been noticed discriminatorily in its fluctuation rate in children, adults to be more bother in male than in the female. Whereas

onychomycosis has a harmful effect on a different region, age groups, type of diseases by great impact of the peripheral vascular, a genetic trait, foot ulcer, diabetes, etc. Side by side to the poor immune system with this satisfaction of disease cure effect of completely undone. Vast treatment distinguishes the elaboration towards the eradication of an infectious agent leading to the normal appearance of the nail, by using certain antifungal along with meta-analysis presenting mycotic and clinical cure rates. The medications include oral allylamine and azole, topical agent and systematic agents. Focusing more on prevention we can get the chance to reduce the disease, hereafter, some new techniques are introduced for the betterment of a remedy.

Introduction:

Onychomycosis is the most common infectious disease of a nail. Infection of fingernails and toenails is enactment by discoloration, lifting of a nail, splitting of nails and thickening of the nail from the nail bed [1]. It is composing about half of all nail abnormalities and most common disease in worldwide. Dermatophyte and non- dermatophyte both fungal species are responsible for this disease. Dermatophyte infection causes 90% diseases due to Trichophyton rubrum and a toenail are infected 80% during these cases of onychomycosis [2]. It is divided into primary and secondary onychomycosis. Fungal invasion infected the undamaged nail in primary onychomycosis and in secondary onychomycosis fungal species affected the abnormal nail which is already infected by the disease. Therefore, primary onychomycosis is rarely contingencies [3]. A fungal culture is a method used for the onychomycosis disease. The species put into the petri dish with non-selective kimming agar. It will be able to differentiate between macroscopic and microscopic morphology of causative pathogens. After the identification these pathogens fungal culture needs 37℃ temperatures for 3 - 5 weeks to grow. Sometimes bacterial growth used to inhibit the fungal culture. Sabouraud’s dextrose agar rapid growth of fungal culture the kimming culture. Both agar has chloramphenicol 50 mg/L, penicillin and streptomycin 40000 IE/L, antibiotics. This is inhibiting the bacterial growth in fungal culture. Dermatophyte needs 26 - 32℃ temperature for 2-4 days to grow. Candida yeast grows at 26-32℃ or up to 37℃ temperature for 2-4 days [4]. Onychomycosis is treating with the therapies of terbinafine and itraconazole. These types of treatment failure in 25 - 50 % patients and cured patients are faced regularly by these infections [5] [6] [7]. These regulations of the infection are due to the resistance of candida in nail [8].

Figure 1: Fungal nail infection



Recent tools used for onychomycosis are nailing histopathology, immunochemistry, flow cytometer and PCR [9]. PCR is more sensitive, rapid and specific test technique used for detection of a small number of samples [10] [11]. Small pieces of nail treat with KOH and PAS (KONCPA) the test shows excellent detection and highly positive result of onychomycosis [12] [13]. Onychomycosis cause clinical problems such as drug are not reach to plate or infected nail due to the separation of the nail from nail bed [14]. When lunula involved in infection abnormal nail grows and produce a damaged and thick plate of the nails which increases the trauma and disease in nails.

Classifications:

Onychomycosis is classified into different classes are distal and lateral subungual onychomycosis (DLSO), proximal subungual onychomycosis (PSO), superficial white onychomycosis (SWO), total dystrophic onychomycosis and endonyx subungual onychomycosis [15].

Table: 1 Classification of onychomycosis

Classes	species	characteristics	Causative pathogens	Reason of infection	references
Distal And lateral Onychomycosis	Dermatophyte	Initiate hyponychium spread along nail Bed due to hyperkeratosis And onycholysis	Candida albicans Trichophton Mentagrophytes Fusarium species	Nail plate is friable and breakdown and break the skin near the Tinea pedis	[16].
		Not infected the nail bed and turn yellow- white and brown-black	T.rubrum C.albicans	Nail cuticle and fold and	[17].
Proximal subungual onychomycosis	Dermatophyte	No paronychia and peripheral vascular and diabetes are present	Fusarium Species T.rubrum	develop secondary paronychia Nail fold And deep	[18].
Superficial white onychomycosis	Dermatophyte	Nail white Other than cream and effected the	Triphyton Soudananse Triphyton violaceum	Penetration of infection Fungus secure thickness of nail without	[16]. [18].

		nail bed		damaged the skin near the Nail bed.	
Total dystrophic Onychomycosis	Dermatophyte	nail plate is totally damaged or destroyed			
Endonyx Subungual onychomycosis	Dermatophyte	nail develop milky appearance and no hyperkeratosis or onycholysis			

Note: Dermatophyte species are involved in all type of these infections of onychomycosis.

Figure 2: distal and lateral subungual onychomycosis

Figure 3: Proximal subungual onychomycosis

Figure 4: white superficial onychomycosis

Figure 5: Total dystrophic onychomycosis

Figure 6: Endonyx subungual onychomycosis

Limitations:

It is caused by dermatophytes like yeast and molds infection. It's effect the nail about 50 % of all negotiations for nail disease. It is usually in males and also spread in both genders with the passage of time [19]. Therefore, men have a higher prevalence rate than women and 9% increase in men with each year of age and this process continue at least 68 years. Both genders have risk at least 1.13 times each year. But in men risk at least 1.27-time increase compared to women. The onychomycosis prevalence rate is different from the 2% to 3% estimate range in the U.S. [20]. Because the new estimates range in the Finnish population is approximately 13% in males. And its prevalence rate worldwide is 10% to 30% [21]. When the mold confines from affected nails such as Candida spp., Aspergillus spp., Alternaria spp. and Cladosporium spp. These are infectious agents and the estimated prevalence rate of non-dermatophyte is 10% to 15% [22]. In this disease, the amplicon sequence is most adequate to identify the infectious agent [23] [24]. Now, a study shows that ITS, Rdna and PCR-based sequence detection rate are 50% [25].

Table: 2 Non-dermatophyte based on culture and PCR-based sequences of nail specimens.

Species of non-Dermatophyte	Culture (n)	PCR based sequence	Culture and PCR based sequence
Candida spp.	27	28	33
Aspergillus spp.	7	4	8
Alternaria spp.	2	2	2
Cladosporium spp.	2	2	2
Total	38	36	45

Note: Different non-dermatophyte species have different value in PCR and culture sequence [26].

In a recent survey, 1038 patients were admitted to a dermatology clinic in Cleveland. It has been a different ratio in humans with different age [19]. In the adult, distal subungual onychomycosis is most common and toenails are mainly common then fingernails. Children attain the fungus of onychomycosis from the dystrophic or traumatic nail abnormality, from parents and environmental contamination [27]. In young age acquire the soles and nails from the genetic susceptibility [28]. These diseases increase with ages.

Table: 3 onychomycosis in individuals.

Age(year)	Chances of disease	References
Adults(18-39 years)	0.6%	[29].
Middle aged(40-64 years)	10-20%	[30].
Alders(up to 64 years)	15-40%	[31].

Note: Different ratio of disease in individuals with different ages.

Harmful effects of onychomycosis:

Onychomycosis having harmful effects on different regions and different type of diseases such as peripheral vascular disease, a genetic trait shared and diabetes involvement. Fungal disease rows in gender discrimination and age differences. More than the age of 60 and less than the age of 19 are having more chances of this infection. When there is more commonness of this onychomycosis in one's partner then there is a number of chances enhanced for the same infection realized in offspring [3]. Admissibly this genetic trait is even discerning on rare cases that it even has the development of dermatophyte infectious result that penetrates deep in tissues level [32]. Hereafter, an unrelenting infectious agent to the skin causes this particular infection due to transplantation of bone marrow by fusarium. Meanwhile, it was observed that a person whoever is having any disease like, HIV, diabetes, have great feasibility to have interacted with this onychomycosis. Narrating more about diabetes myelitis reason for adopting this infection could link to the abnormal circulation where it faces foot ulcer or other diabetic foot syndromic

effect [33]. A patient who is not so well recognized immune system or poor to respond to infection may have this feet disease again and again even though, that is a cure for once could be replaced again with same worsening effects along with the logic of referring to genetic trait [34]. Experimentation work showed that the minimum inhibitory concentration for specific fungal strains was colonized, and in result show resistance to the drugs used against it and observed to be resistant to crosslink infection of antifungal agents [35]. Whereas with distinguishing focus on the particular is of infecting an agent may lead feet from deformed or unrelenting to originals shaped to sever feet pain with untreated problems spreading to nearby skin areas for more disastrous consequences. It can even create cracks on the skin with swollen and ruptured, tender skin showing red in color and make ease for bacteria to enter in the skin this condition of the skin is cellulitis. The fungus can move even from reproductive organs, genital in an animal that causes itching [36]. Transferable infection with prominent observation is that it shifted from one finger to other forming as discolored, broken part to the next finger to become fungal, linking it with pus is noticed the skin is becoming infected. This disease has a strong harmful effect where the nail is cut off from the body and it can either affect more to toes than to fingers so limiting to extend level nail could be removed with three different ways. A complete nail is removed has the terminology of avulsion if any specific part more infected in the nail is removed that is debridement, where the nail is numb to reduce pain by treating it with anesthetic [37]. If moving to a painless mean of removing a nail, treatment is about putting indulgences of chemicals, urea for days along with the aspect that if medication is not enough then the use of laser treatment is considered in progress.

Treatment:

Onychomycosis treatment is an object at the elimination of causative agents and improving the appearance of nails. Onychomycosis is believed to be a cosmetic problem and can lead to the foot ulcer in a diabetic patient [38] and cellulitis [39]. Cellulitis is an inflammation of subcutaneous connective tissue. Eradication of infection and return to its normal appearance but it is not easy because the nails are made up of keratin, which is nonvascular and impervious to many agents [40]. Another reason is the poor drug delivery to the nail that effect, the treatment may not appear for a year. Treatment manner includes topical antifungal, oral, a combination of therapies and surgical treatment. Cure rate remains slow because a high rate of relapse seen after successful treatment. Treatment also has varying effectiveness, depend on cure parameter. Mycotic cure indicates that no organism finds on culture and microscopy. Clinical cures refer to the improvement of nail appearance in 80% to 100% of the nail [41]. The mycological cure rate

is 30% better than the clinical cure rate. Complete cure indicates that clinical or mycotic cure has been attained.

Oral Allylamine and Azol:

Antifungal used for the treatment of onychomycosis. Antifungal from allylamine and azol is used as an oral medication for the treatment of onychomycosis. The azol class includes Diflucan, itraconazole, and ketoconazole. Ketoconazole is used very rarely because of hepatotoxicity and drug interaction. The allylamine includes Lamisil [3] [42]. A meta-analysis for the treatment of onychomycosis shown that Mycotic cure rate was 59% for itraconazole with continuous dosing, 635 for itraconazole with pulse dosing and 48% for Diflucan [14]. The clinical cure rate was 70% for itraconazole with pulse dosing and with continuous dosing, 41% for Diflucan and 66% for Lamisil. The common adverse effect includes gastrointestinal problems, a headache, rashes, and ventricular dysfunction. The use of an agent discourages in patients with renal or heart disease, with liver and in those who received medication in which there may be significant drug-drug interaction.

Topical Agent:

Various topical agents are used for the treatment of onychomycosis. These topical agents have few cautions and no drug-drug interaction. Ciclopirox 8% solution is the only topical agent available in the USA for the treatment of onychomycosis. It has some adverse effect include stinging at the application site, itching, and burning. It is a hydroxy pyridine antifungal design as the nail polish [43]. It may use in those patients who have less than 50% distal nail affected, cannot take oral antifungal and no lunar involvement [44]. Ciclopirox has clinical cure rate 6% to 9 % and mycotic cure rate 29% to 36% [3]. It is not used in patients younger than 12 years [14].

Systematic agent/therapy:

The three drugs are licensed for used in onychomycosis are griseofulvin, terbinafine, itraconazole. Terbinafine and itraconazole have been studied above.

Griseofulvin:

Griseofulvin is weak fungi static, acts as an inhibitor by inhibiting fungal cell wall synthesis, the nucleic acid synthesis and arresting cell division [45] [46]. It is the only antifungal used in children with onychomycosis and available in tablet form, requires to be taken with fatty food to increase its absorption. The recommended dose in adult 500 mg daily for 6 to 7 months in fingernail infection and 12 to 18 months in toenail infection. The mycological cure rate is 70% in fingernail infection but the disappointing drug in toenail infection, whereas cure rate only 30-40

% [47]. Side effects include rashes nausea 8-15% of patients.

Table 4.Commonly prescribed medication for the treatment of onychomycosis.

	Cure rate%				
Medication	Dosing	Mycotic	Clinical	Targeted species	Potential adverse effects
Ciclopirox 8% solution (nail polish)	Apply once a day to affected nail and underside of nail	29 to 36	6 to 9	Candida species dermatophytes	Nail shape changes, burning sensation, erythema of proximal nail fold, nail discoloration, ingrown toenail.
itraconazol	Continuous dosing: 200 mg orally 12 week once a day in toenails infection and six week in fingernails. pulse dosing: 200 mg two times a day for one week per month, three month in toenail infection, two month in fingernail	69 63	70	Aspergillus species, candida species, dermatophyte, non-dermatophyte, molds	Vomiting, elevated transaminase, nausea, rash and hypokalemia.
Lamisil (terbinafine)	250 mg orally once a day 12 week in toenail infection, six week in fingernail.	76	66	dermatophyte, non-dermatophyte, molds and some yeast	Rash, headache, gastrointestinal problem

Diflucan (fluconazole)	100 to 300 mg orally every week, 6 to 12 month in toenail infection, 3 to 6 month in fingernail.	48	41	Candida species	Vomiting, abdominal pain, rash, diarrhea, headache, and nausea

Note: it contains information about some drugs with dosing, cure rates, targeted species, and potentially adverse effect. Itraconazole and terbinafine also considered in the category of the systematic agent [42] [48] [3] [14].

Prevention:

Onychomycosis affected the children in the age of 6 years and not effected under the 12 years. It is most common in the age between 12-18years [49] [50]. In younger children onychomycosis is due to faster nail growth, less exposure of pathogens in gyms and public pool, lower tinea pedis and fewer traumas [51]. Children who have genetic disease develop the exposure of dermatophyte infection. Hence, prevent from wearing athlete foot wares, walking without barred footed in locker rooms, shared household with each other [52], Feet keep dry and cool, apply spray or powder under the shoes at least one time in a week and discard old shoes not used again, apply proper medication on foot nail and toenails.

Future aspects:

Now antifungal focus on the formulation of new agents has been developed in recent years. Tavaborole is borne based agents are approved by the U.S. for treatment of onychomycosis which is caused by T.rubrum and T.mentagrophytes [53]. It inhibits the protein synthesis and disappearance of fungal cells growth. It is applied 16% dose on nail plate than ciclopirox [54]. New techniques of laser light devise, and carbon dioxide laser is applied for control or treat the onychomycosis disease. Carbon dioxide laser is highly specific than other and different therapies are also determined for this purpose which is less the resistance of nail fungus. These are UV light therapy, photodynamic therapy, and dual-wavelength 870 -/930-nm laser. Dual wavelengths are modern techniques are given 100% result for this disease [55]. Photodynamic is shown 50% result to reduce the growth of fungus and UV light are not feasible because it does not show resistance in T.rubrum. The UV light does not absorb in nail until it is 320 nm or greater.

Conclusion:

Persistent onychomycosis might be growing the charges of fitness care about oneself. In this observe, an excessive percent of patients imparting another disease except for fungal infection

alert, from the reality that care and regular checkups should be focused by means of clinicians in not only geriatric people but of all ages facing the problematic infection. Meanwhile, examinations and traditions are fundamental exceptions of tools or therapies to provide accurate prognoses earlier than starting any quick response to make it vulnerable, so remedy samples have to be carried out on a routine basis.

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