Review Article

Nail Society of India Recommendations for Treatment of Onychomycosis in Special Population Groups

Abstract

Onychomycosis (OM) is a difficult-to-treat condition, especially considering the limited armamentarium of antifungal drugs, need for prolonged treatment, and poor compliance. This problem is further confounded while treating OM in special populations such as children, elderly, immunosuppressed patients, pregnant or lactating women, and patients with chronic liver or kidney disease. In the absence of standardized treatment guidelines, the antifungal therapy is either withheld or compromised, as it is largely governed by personal preferences or based on anecdotal reports. Hence, an expert group of the Nail Society of India worked towards drafting guidelines based on established literature and inputs from experts, with practical recommendations for the treatment of onychomycosis in special population groups. An extensive analysis of available English language literature on onychomycosis in special populations, published during a 10-year period (2014–2023 until date) was done. The available studies and reports were evaluated, cross-references read, and evidence compiled, graded, and discussed by the expert group to derive consensus recommendations for practice. The evidence and recommendations based on it are presented in a narrative format to guide treatment choices when dealing with population groups with special considerations.

Keywords: *Chronic kidney disease, chronic liver disease, geriatric, immunosuppression, pediatric, pregnancy*

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Introduction

Onychomycosis (OM) is a difficult-to-treat onychopathy. The number of efficacious drugs available are limited, and outcomes are sub-optimal many a times. The major potential causes are prolonged treatment duration and the asymptomatic benign nature of the disease, associated with overall poor compliance and drug-associated adverse effects. The scenario gets further complicated in special population groups, such as pediatric and geriatric populations and pregnant and lactating mothers, to name a few, where cautious drug administration is warranted. Treatment in such cases is withheld for indefinite periods, or if administered, it is done in a highly compromised fashion, largely based on personal preferences. Good quality evidence in these populations is lacking because these patients are generally excluded from the drug trials for ethical reasons. Available treatment recommendations for OM offer very limited insight into such special cases. To bridge this gap, an expert group of the Nail Society of India (NSI) reviewed the literature extensively and framed practical recommendations for the treatment of OM in pediatric, geriatric, pregnant, lactating, diabetic, or immunocompromised patients and those with organ compromise, psoriasis, or peripheral vascular disease.

Materials and Methods

The NSI expert group first identified special population groups in which treatment of OM is challenging. A PubMed database search was done by KM, CG, and DJ for published literature in English language for these groups. The search was filtered to include case reports, clinical studies and trials (all types), comparative studies, guidelines (including pragmatic), reviews (including systematic), and meta-analysis. The other filters applied included species (human) and duration (2014–2023). The article titles and abstracts were read, and full texts of

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relevant articles were retrieved. Relevant cross-references were also studied. The collected data was assigned levels of evidence (LOE) as per the Oxford Centre for Evidence-Based Medicine Levels of Evidence (OCEBM) scheme [Table 1].[1] Treatment-related practice recommendations were then derived and discussed by the authors to assign Grades of Recommendation (GOR) [Table 2].[1]

Results

The PubMed search results for searched keywords are summarized in Table 3. The data were collated and analyzed through virtual discussion between expert group members to finalize practice points. For entities with very limited and poor-quality scientific data, personal experiences of the group members were added (LOE V, GOR D). The same are presented below in a narrative format.

Onychomycosis in Children

The prevalence of childhood OM ranges from 0.35% to 5.5% worldwide and is reported to cause 15.5% of all nail dystrophies in children.[2-4] In recent times, an increase in its incidence has been noticed in children, possibly due to the use of occlusive synthetic footwear, communal locker rooms, public swimming pools, and inoculation from affected family members. It is generally believed that children are at a lower risk of developing OM due to a faster nail growth, a lower surface area of the nail unit, and lower exposure to pathogens and trauma.[2] It is however more commonly seen in children with Down's syndrome or immunodeficiencies such as HIV-AIDS and chronic mucocutaneous candidiasis (CMC).[3]

Dermatophytes are considered the most common cause of onychomycosis in children, with *T. rubrum* being the most common organism isolated from both finger and toenails. Candidal and non-dermatophyte onychomycoses are less common.[3] Dermatophyte nail infection is commonly seen after the age of 6 years, with only a few sporadic cases being seen in less than 2 years age.[3] The incidence increases after adolescence. Children with OM should always be examined to find other foci of infection, especially tinea pedis or capitis. Additionally, all close contacts should be screened and assessed for dermatophyte infections. Among Candida species infections, *C. albicans* and *C. parapsilosis* are the most frequently isolated species, and onychodystrophy may be associated with perionyxis.[5] An underlying immunodeficiency should always be suspected in such cases. The need to confirm diagnosis before starting therapy in children has been emphasized repeatedly.

Treatment choices in children are mostly off-label as there are no USFDA (Food and Drug Administration, USA)-approved drug recommendations for pediatric age group. Table 4 summarizes the drugs used in pediatric OM, their doses, and USFDA status. A systematic review investigating the efficacy and safety of antifungals (oral and topical) in children with OM found oral itraconazole to have the highest clinical cure rate (94%), followed closely by topical ciclopirox (mycologic cure of 70%).[6] Since the adverse events noted in children are similar to those in adults, it could be suggested that as per the recent recommendations, evaluation of baseline liver function should be done in children treated with oral drugs, along

Table 1: Levels of evidence from OCEBM

Level of evidence	Type of study
I	Systematic reviews of RCT or individual RCT (with narrow confidence interval)
II	Systematic reviews of cohort studies or individual cohort study
III	Systematic reviews of cohort studies or case-control studies, individual case-control study
IV	Case-series and poor-quality cohort and case-control studies
V	Expert opinion

Table 2: Grades of Recommendation

Grade	Level of evidence
A	Consistent level 1 studies
B	Consistent level 2 or 3 studies or extrapolations from level 1 studies
C	Level 4 studies or extrapolations from level 2 or 3 studies
D	Level 5 evidence or troubling inconsistent or inconclusive studies at any level

Table 3: Pubmed search results

Keywords used	Number of articles
onychomycosis AND treatment AND [children OR pediatric]	51
onychomycosis AND treatment AND [geriatric OR elderly]	193
onychomycosis AND treatment AND pregnancy	2
onychomycosis AND treatment AND (lactation OR breastfeeding)	2
onychomycosis AND treatment AND diabetes	35
onychomycosis AND treatment AND (chronic kidney disease OR chronic renal disease)	1
onychomycosis AND treatment AND chronic liver disease	3
onychomycosis AND treatment AND immunosuppression	27
onychomycosis AND treatment AND HIV	9
onychomycosis AND treatment AND (carcinoma OR chemotherapy OR Malignancy)	37
onychomycosis AND treatment AND nail psoriasis	36
onychomycosis AND treatment AND peripheral vascular disease	4
onychomycosis AND treatment AND (heart or cardiac)	4

Table 4: Drugs and dosages used for pediatric OM

Drug	Dose	FDA approval age
Efinaconazole	Once daily Toenails 48 weeks	>6 years
Tavaborole	Once daily Toenails 48 weeks	>6 years
Ciclopirox solution	Once daily Toenails 48 weeks	>12 years
Terbinafine	250 mg tab: • <20 kg-62.5 mg/day • 20-40 kg-125 mg/day • >40 kg-250 mg/day Terbinafine granules (125 mg or 187.5 mg packet) • <25 kg 125 mg/day (1 packet of 125 mg) • 25-35 kg 187.5 mg/day (1 packet of 187.5 mg) • >35 kg 250 mg/day (2 packets of 125 mg)	Off-label use in OM. Terbinafine granules approved for tinea capitis in >4-year-old children
Itraconazole	5 mg/kg/day	Off label use in OM
Fluconazole	6 mg/kg/week	Off label use in OM FDA-approved for candidiasis in 6 months to 13 years of age

with monitoring in the same manner as in adults.[7] Teenagers need to be counseled to avoid alcohol ingestion while receiving systemic treatment.

Topical treatment in children

Topical therapies are known to work well in children and are the preferred mode of treatment, especially in cases with superficial white OM (SWO) or mild to moderate subungual OM without onycholysis or matrix involvement.[8,9] Children have thinner and faster growing nails, which are considered more responsive to topical therapy than adult nails. Other advantages of topical therapy in children include better compliance (easier to apply than to make them swallow!), no requirement for dose adjustments, and lesser parent apprehensions and need for counseling.

Friedlander and colleagues demonstrated the efficacy of topical ciclopirox for non-matrix toenail OM in pediatric age groups. At the end of 32 weeks, the mycological cure rate was 77% in treated patients as compared to 22% in the control group.[9] Though it has received approval for use in children more than 12 years of age, ciclopirox has been found effective even in infants.[10] Amorolfine nail lacquer has also shown favorable response rates in a few case reports.[11] However, no trials of its usage have been found in the pediatric population.

The newer FDA-approved topical agents for adults have shown promising results in pediatric OM and are deemed better than ciclopirox. Unlike nail lacquers, these are in solution formulation, which has higher nail penetration and does not require frequent debridement. In future, they could be the practical alternatives to oral antifungals for the treatment of mild to moderate OM in children. Their potent activity against dermatophytes and excellent tolerability could make them the treatment of choice even in severe OM. Efinaconazole demonstrated high cure rates in the pediatric population as compared to the adult population. It had a mycological cure rate of 65% and a complete cure rate of 40% at week 52 following a 48-week daily application.[12] It has been FDA-approved for use in children >6 years of age. Similar encouraging results have been seen with tavaborole. In an open-label study involving pediatric patients (6–17 years of age) with distal and lateral subungual OM (DLSO) affecting ≥20% of the great toenail, tavaborole once daily application for 48 weeks achieved a complete cure rate of 8.5% and an almost complete cure rate of 14.9% at week 52.[13] Importantly, this study found tavaborole to be safe in the pediatric population. Prophylactic use of topical antifungals should also be ensured post systemic therapy to prevent chances of recurrence. Gupta *et al*. recommended twice weekly use of topical antifungals for 2–3 years for the same.[8]

Practice points: *We recommend using topical antifungals in children in the setting of SWO or mild to moderate DLSO without matrix involvement* (LOE III, GOR B). The *choice of agent (ciclopirox vs amorolfine) can be similar to that recommended in adults in the previous NSI recommendations.[7] If and when the newer antifungals like efinaconazole and tavaborole are available in India, they should be preferred.*

Systemic treatment in children

A systematic review of 26 studies pertaining to treatment of OM in children included five clinical trials evaluating oral treatment (terbinafine, itraconazole, fluconazole, and griseofulvin). It showed an overall 70.8% complete cure

rate, with a favorable safety profile, thus establishing the role of oral treatment in children.[14] However, etiological species, severity of onychomycosis, and dosing need to be kept in mind before initiating systemic therapy in children.[15]

Terbinafine for children is adjusted based on their weight [Table 4]. In the systematic review by Gupta *et al.*, terbinafine was found to have a complete clearance rate of 78.8%,[14] which is higher than that reported in the meta-analysis for adult OM. It is used off-label in children with OM, though terbinafine granules are FDA-approved for children >4 years of age with tinea capitis. These are not available in India. Combination therapy [terbinafine and topical antifungal (ciclopirox or amorolfine)] has shown better efficacy with higher cure rates up to 90%.[16]

Itraconazole pulses for 3–5 months have been reported to be both effective and safe for OM in children.[17] The dosage to be used is 5 mg/kg/d for 1 week of each month. The recommended duration for pulses is the same as in adults (two pulses for fingernails and three for toenails). A review of itraconazole use in infants with superficial dermatophytosis (5 mg/kg/day) and systemic mycoses (10 mg/kg/day) found it to be a safe and effective drug with few serious adverse effects, making it the second-line systemic therapy in the pediatric age group.[18] While it is not FDA-approved in children, the British Association of Dermatologists recommendations defined "terbinafine or itraconazole as first-line treatments for onychomycosis in children, with terbinafine being preferred".[19]

Fluconazole and griseofulvin have been recommended as second-line agents in children with OM. Fluconazole is USFDA-approved in children aged 6 months to 13 years (for candidiasis). Griseofulvin is the only systemic antifungal licensed for use in children; however, it is not recommended for OM as first-line therapy due to longer duration of treatment and lower efficacy.[20] In India, oral formulations of fluconazole (50 mg/ml oral suspension) as well as itraconazole (10 mg/ml oral solution) are available for pediatric use, which is an added advantage in children unable to swallow pills.[20]

Practice points: *Oral therapy in children may be required when multiple nails are involved, matrix is involved, or topical penetration is expected to be sub-optimal. In children requiring oral therapy, terbinafine (weight-based dosing) should be preferred in dermatophyte OM and itraconazole pulses (weight-based dosing) in non-dermatophyte mold or candidal OM (LOE III, GOR B). In children with CMC or immunodeficiencies, low threshold should be kept for starting oral antifungals (LOE V, GOR D). Fluconazole is the preferred agent in this category (LOE V, GOR D). Appropriate baseline monitoring of liver function should be done like in adults as data regarding their safety in children are limited (LOE III, GOR B).*

Device-based and other therapies in children

There are limited data on the safety and efficacy of lasers in children.[3,8] Their use in children cannot be recommended.

Onychomycosis in Elderly

There is a higher prevalence of OM in the elderly with almost 50% people over 70 years of age, reported to be affected.[19] Dermatophytes and nondermatophyte molds (NDM) are more common causative agents in this age group. The presence of comorbidities, recurrent and cumulative trauma, impaired wound healing, decreased immunity, and peripheral vascular compromise are all contributory towards this. This, along with polypharmacy and potential of drug interactions, makes the elderly more prone to treatment-related adverse effects as well as compromised outcomes. There is a paucity of literature assessing efficacy and safety of antifungals in the elderly. Widely practiced management options for OM in elderly include no therapy, palliative treatment with mechanical or chemical debridement, topical antifungals, oral agents, or a combination of these modalities.

Baran *et al*. have suggested that in the elderly, treatment should be topical antifungals with or without chemical (40% urea) or mechanical nail avulsion.[21] All topicals including the newer agents can be safely used in the elderly. However, in patients needing systemic therapy, weekly fluconazole 300 mg or terbinafine (250 mg twice daily in a pulse form for 1 week every month) can be given. Mostly, elderly patients receive only local treatment such as mechanical intervention or chemical nail removal, which carries no risk to the ischemic toe and has an added advantage of involvement of another person to apply the treatment.[22]

Gupta *et al.* conducted a randomized comparative study for OM in patients aged >60 years.[23] They evaluated continuous terbinafine (250 mg/day for 12 weeks) and pulse itraconazole (200 mg twice a day for 1 week, given for 3 pulses). At 18 months, the mycologic cure rate and clinical efficacy for the terbinafine and itraconazole groups were 64.0% and 62.0% versus 62.7% and 60.8%, respectively, with no statistically significant difference. Compliance was good, and the adverse effects were mild and transient.[23] Kaul *et al.* recommended terbinafine as the first-choice treatment (4 weeks extension of treatment in cases of inadequate response) and itraconazole pulse therapy as the second line (one extra cycle in case of inadequate response).[20] Fluconazole and griseofulvin may only be used as alternative therapy. Fosravuconazole is a novel oral antifungal drug developed and approved for the treatment of tinea unguium in 2018.[24] Its excellent oral absorption has enabled short-duration therapy of 3 months. It is a weak inhibitor of cytochrome P450 enzyme; hence, it has virtually no drug interactions. Therefore, it can be considered as a safer option for elderly patients.[24] The drug is currently not available in India.

Practice points: *Topical therapy for OM should be the first line of therapy in the elderly age group for patients with a limited number and extent of nail involvement. In elderly patients requiring systemic therapy, terbinafine should be the preferred drug, especially in patients on polypharmacy, because of less potential for drug interactions (LOE III, GOR C). Itraconazole may be preferred in cases with candidal OM, keeping in mind potential drug interactions. Chemical nail avulsion or debridement may be preferred in appropriate situations (LOE IV, GOR C).*

Onychomycosis in a Pregnant Patient

Due to the need to avoid systemic drugs, especially in the first trimester, there are no trials or formal guidelines for the use of oral antifungals in pregnancy. The long-standing nature of the disease and its slow progression mean that pregnant women should be treated with topical agents as far as possible. Systemic agents are reportedly best avoided during pregnancy.

Among the topical agents, topical ciclopirox 8% (Pregnancy Category B) and amorolfine 5% (not USFDA-approved) are considered safe for use throughout pregnancy. However, there is a lack of human studies. Luliconazole is labeled as Pregnancy Category C due to a lack of adequate and well-controlled studies in pregnant women. Embryo toxicity has been noted with efinaconazole and tavaborole in animal studies, though there is a lack of human studies. However, this toxicity reportedly occured at much higher doses than those recommended for human use.[20]

Terbinafine is the only Category B systemic agent efficacious in OM. Even then, data on its use in pregnancy are not available and its use is not recommended. In a registry-based Danish cohort study, including 891 oral terbinafine-exposed pregnancies, 3174 topical terbinafine-exposed pregnancies, and 40,650 unexposed pregnancies (controls), there were no significant differences in the risk of major malformations or spontaneous abortions between the three groups.[25]

Itraconazole is a Pregnancy Category C agent. In a systematic review and meta-analysis, the administration of itraconazole during pregnancy was not associated with any increased risk of spontaneous abortion or stillbirths. However, the frequency of ocular defects was considerably higher than the rate reported in the general population.[26] Therefore, itraconazole should be avoided during pregnancy.

Fluconazole is classified as a Category D drug as it has been associated with birth defects in animals and humans.[27] In a population-based study, low doses (<150 mg) of oral fluconazole during early pregnancy were associated with an increased risk of abortions and high doses (>150 mg) were associated with an increased risk of cardiac septal closure anomalies compared with no exposure to the drug.[28]

Various mechanical modalities (cutting, abrading, filing, partial avulsion) can be used as adjunctive therapy in cases with more severe or painful OM,[20] even though their efficacy is not backed by data. According to Ricardo *et al.*, lasers can be safely used in pregnancy and lactation.[27] The safety of carbon dioxide and Nd: YAG 1064 nm lasers during pregnancy has been determined in a few studies pertaining to genital warts.[29] However, there are no studies of their use in OM. These can be used as adjunctive treatment for OM, if affordable and available.

Practice points: *Topical monotherapy (mainly ciclopirox 8%) is recommended in pregnant patients with OM. These may be combined with mechanical or destructive modalities. Oral antifungals should be avoided (LOE II, GOR B).*

Onychomycosis in a Lactating Patient

All oral antifungals are excreted in milk. Hence, their use is not recommended in lactating females for obvious reasons. Excretion of topical antifungals into breast milk has not been determined.[27] Though there are no studies on mechanical debridement and use of lasers in lactating females, some authors opine that it can be used as a treatment modality.

Practice points: *It is recommended to use topical antifungals in lactating females (LOE II, GOR B). It can be combined with mechanical or laser-based modalities, if deemed necessary.*

Onychomycosis in a Diabetic Patient

As compared to the general population, diabetics, especially men, are 2.5–2.8 times more likely to develop OM, which commonly affects the toenails.[30] Predisposing factors include sensory neuropathy, poor glycemic control, microangiopathy with resultant ischemia, and impaired host defenses. Dogra *et al*. reported yeast (48.1%) to be the most common causative agent for OM in diabetics, followed by dermatophytes (37%) and NDM (14.8%).[31] Gupta *et al.* also found that elderly and diabetics had the highest rate of yeast OM.[32] Treatment in diabetic patients is both difficult and prolonged. More than any other sub-population of OM, this one requires a three-pronged approach, with oral antifungal therapy being supplemented with mechanical measures and patient education.

Topical therapy in diabetics is considered appropriate for patients with mild-to-moderate infections or where the risk of drug interactions is considered high. For patients with severe OM, multiple nail involvement, and spread to other areas, more aggressive treatment is required. In such a scenario, a combination of topical and systemic therapy is preferred to achieve more rapid and prolonged cure.[32]

Terbinafine is considered the preferred oral agent in this population because of a lower risk of adverse events or drug interactions.[33] Itraconazole, which is contraindicated in congestive heart failure and has potential for drug interactions,

is not a preferred therapy in diabetics who are more prone to cardiac disease and may be on other drugs as well.

Physical debridement of thick sharp mycotic nails is strongly recommended as sharp nails may be a source of neglected foot injury in these patients. The importance of proper foot care and need for self-examination of foot daily should be emphasized in patients with diabetes.

Practice points: *Combine topical and mechanical measures in diabetic patients with OM. If required, oral terbinafine is the preferred systemic agent in diabetic patients (LOE III, GOR C).*

Onychomycosis in the Immunosuppressed

There is higher prevalence of OM in patients with immunosuppression attributable to various causes, including human immunodeficiency virus (HIV), primary immunodeficiency, transplant recipients, or chemotherapy. In patients with HIV infection, the prevalence of OM has been found to correlate with CD4+ cell counts below 450 cells/mm^3.[34] There are no recent studies regarding the prevalence in immunosuppressed patients; however, a study done in 2000 showed *T. rubrum* to be the most common pathogen, with rare cases being caused by NDM and Candida.[35] In the early 1990s, proximal subungual OM (PSO) dominated the clinical presentation of OM in HIV-positive individuals; however, with the use of oral fluconazole for oropharyngeal candidiasis and the use of anti-retroviral therapy therapy, the prevalence of PSO has significantly declined.[21]

Therapeutic challenges in this population range from a risk of incomplete eradication of the organism, toxicity of the drugs administered systemically, and growth of more resistant species. Again, there is not much literature regarding the treatment of OM in immunosuppressed individuals. Terbinafine or fluconazole are considered the preferred therapeutic options as itraconazole is associated with a higher risk of drug interactions with antiretroviral drugs, immunosuppressants, or chemotherapeutic agents that the patient may be on.

Practice points: *Since immunosuppressed patients are at a greater risk of spread of infection to other nails or body parts, it is recommended to use oral antifungals for OM, especially in cases with multiple nail involvement, matrix involvement, or PSO. Terbinafine is the preferred oral drug (LOE V, GOR D). Mechanical measures should be avoided due to other co-morbidities and associated risks.*

Onychomycosis with Nail Psoriasis

Klassen *et al.* reported a higher prevalence of OM in patients with psoriasis as compared to the general population (18% vs 9%).[36] Gupta *et al.* also reported a 56% higher incidence of OM in patients with psoriasis versus non-psoriatics.[37] Natarajan *et al.* found investigative evidence of OM in 23 out of 48 patients with psoriatic nail change.[38] Kaul *et al.* reported histological evidence of OM in 26% patients with nail psoriasis.[39] Higher predisposition may be due to alterations in capillaries, leading to a natural loss of defense against microbes, or by the presence of a favorable environment secondary to nail detachment. On the contrary, some authors argue that the rapid turnover seen in psoriatic nails may actually be protective against the development of OM. Alves *et al.* highlighted the possible role of immunosuppressive therapy (mainly methotrexate) as a predisposing factor for development of OM in psoriatic patients; however, this needs to be investigated.[40] Though there are no published studies on treatment of OM in psoriatic patients, there are a few reports of exacerbation and even *de novo* development of psoriasis in patients given terbinafine for cutaneous dermatophyte infections.[41]

Psoriatic patients with nail lesions should be checked for clinical and microbiological evidence of secondary OM by doing PAS staining of nail clipping with demonstration of invading fungal hyphae. If present, such cases should be treated with systemic antifungals, preferably itraconazole rather than terbinafine, to avoid potential aggravation of psoriasis. Topical steroids applied on the nail unit should be avoided in such cases as they may aggravate fungal nail infection.

Practice Points: *It is recommended that patients with psoriatic nail disease be assessed for clinical signs suggestive of OM, further confirmed on investigations. They are best treated with systemic itraconazole in view of the safety as well as the concomitant fungal flora expected (LOE V, GOR D).*

Onychomycosis with Compromised Organ Function

Chronic kidney disease

In a study by Gupta *et al.*, the prevalence of dermatophyte toenail OM was 11.93% in patients on dialysis and 5.17% in patients with renal transplant.[32] Patients on dialysis had the highest prevalence of dermatophyte OM.[32] While planning treatment in such patients, the potential for drug toxicity with systemic agents should always be considered. Terbinafine clearance is reduced by approximately 50% in patients with renal impairment (creatinine clearance <50 mL/min) as compared to healthy volunteers. Hence, it should not be used in patients with renal impairment or used in half the dose, if necessary, only in consultation with a nephrologist. Itraconazole should also be used with caution in patients with renal dysfunction.[42,43] However, it can be used, if deemed necessary, as no dose adjustment is needed if glomerular filtration rate is more than 10 ml/min/1.73 m^2 of body surface area.[44] There are no specific studies done in this population group regarding topical or mechanical forms of treatment.

Practice points: *We recommend the use of topical antifungals in these patients as first-line management (LOE V, GOR D). Systemic therapy should always keep in mind the other*

concomitant drugs and renal function and should always be in consultation with a nephrologist (LOE V, GOR D).

Chronic liver disease

Itraconazole and terbinafine, being mainly metabolized by liver, are not recommended for use in patients with chronic liver disease.[21,42] Fluconazole, if needed, may be used with caution. Again, there are no specific data on the use of topical, mechanical, or device-based therapies in these patients.

Practice points: *It is recommended to use topical antifungals in these patients as first-line management (LOE V, GOR D). Systemic therapy should always keep in mind the other concomitant drugs and liver function and should always be in consultation with a gastro-enterologist (LOE V, GOR D).*

Cardiac disease and hypertension

Itraconazole is reported to have negative ionotropic effects, and the prescribing information for oral itraconazole includes a boxed warning describing the risks for congestive heart failure, cardiac effects, and drug interactions.[45] Therefore, itraconazole should be avoided in patients with the presence or history of congestive heart failure or coronary artery disease. Terbinafine has been used as an oral therapy in the literature and if needed it can be used cautiously.[46,47]

Practice points: *It is recommended to use topical antifungals in these patients as first-line management (LOE V, GOR D). Oral terbinafine as systemic therapy, if required, can be added, and should always be in consultation with a cardiologist (LOE V, GOR D).*

Onychomycosis with Peripheral Vascular Disease

Vascular insufficiency can be a result of either venous insufficiency or peripheral arterial disease. Though there is scarce literature on prevalence or treatment of OM in these situations, it is believed that any compromised vascular function may increase its prevalence.[48] In such situations, treatment should be initiated at the earliest to prevent further spread of the fungal growth. These situations also pose a therapeutic challenge because of the inability of the drugs to achieve adequate concentration at the target site, further leading to higher chances of treatment resistance. In a study by Shemer *et al.*, nail deformities were seen in 84% of patients with chronic venous insufficiency, out of which 75% had OM. When these patients were treated with itraconazole pule therapy for 4 months, complete cure was achieved in only 25% of patients (compared to 60–70% cure rates achieved generally with itraconazole pulse therapy). It was also seen that patients who achieved good cure rates were younger in age and had chronic venous insufficiency of shorter duration.[49] This means that treatment should be started at the earliest and should be prolonged in such situations, though there is lack of any data to support this. In addition, patients, especially the older age group, should be counseled about the chances of incomplete cure, despite adequate treatment. The use of oral or topical antifungals would depend on the criteria already defined; however, in these patients, clinical monitoring should be more frequent. Regarding mechanical measures or debridement, decision needs to be taken after evaluating the possibility of poor healing in these patients.

Practice points: *It is recommended to use topical and systemic antifungals in these patients as recommended*

Table 5: Summary of treatment recommendations for OM in special population groups

Special population	Preferred agent	LOE, GOR
Pediatric (SWO or DLSO without matrix involved)	Efinaconazole, tavaborole >ciclopirox, amorolfine	LOE III, GOR B
Pediatric patients (multiple nails affected, matrix involvement, or PSO)	Terbinafine for dermatophyte OM Itraconazole for NDM Fluconazole for candidal OM	LOE III, GOR B
Geriatric patients	Topical > systemic therapy (if likely to be successful) (Terbinafine > itraconazole)	LOE III, GOR C
Pregnant women	Topical (ciclopirox > amorolfine)	LOE II, GOR B
Lactating	Topical (ciclopirox > amorolfine)	LOE II, GOR B
Diabetic	Topical + oral (terbinafine preferred) + Mechanical measures	LOE III, GOR C
Immunosuppressed	Oral (terbinafine preferred)	LOE V, GOR D
Psoriatic nail	Oral (itraconazole preferred)	LOE V, GOR D
Chronic kidney disease	Topical agents preferred If required, oral itraconazole preferred	LOE V, GOR D
Chronic liver disease	Topical agents preferred	LOE V, GOR D
Cardiac disease	Topical agents preferred If required, oral terbinafine preferred	LOE V, GOR D
Peripheral vascular disease	Same as general population; however, therapy should be prolonged	LOE V, GOR D

for the general population. However, the need for closer follow-up or prolongation of therapy should be carefully weighed (LOE V, GOR D).

Table 5 summarizes the preferred agents in different special populations.

Conclusions

Onychomycosis can be a more formidable adversary in certain special population groups because they are more prone to either the infection or treatment related adverse effects. There is a lack of well-controlled studies guiding treatment choices in such groups. Treatment needs to be individualized taking into account specific population characteristics. These recommendations for treatment of onychomycosis in special populations take into account available literature as well as practical experience of the expert group in dealing with such cases.

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Conflicts of interest

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