Clinico-Mycological Study of Onychomycosis and Pattern of Drug Resistance

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ABSTRACT

Introduction: Onychomycosis is a fungal infection of the toenails or fingernails that may involve any component of the nail unit, including the matrix, bed, or plate. Onychomycosis is caused by dermatophyte fungi, non dermatophyte moulds and yeasts. Prevalence rates for OM varying from 3 to 5% have been found in most studies; however, a few reports suggest a higher prevalence of even up to 26% in the general population. Hence through this study an attempt was made to identify the various clinical patterns of onychomycosis and to identify pattern of drug resistance in onychomycosis.

Material and methods: The proposed study was carried out in Outpatient Department of Dermatology Venereology and Leprosy, Rohilkhand Medical College and Hospital, Bareilly, a tertiary care hospital in western Uttar Pradesh for one year (November 2017- October 2018) on patient showing nail changes suggestive of onychomycosis, using direct microscopy using potassium hydroxide. The culture medium SDA with chloramphenicol was used. Sensitivity to Terbinafine, Fluconazole, Itraconazole and Griseofulvine was studied.

Result: The most common pattern of onychomycosis seen was distal lateral subungual onychomycosis. Pattern of drug resistance is maximum with Griseofulvin (49%) and least with Terbinafine (20%).

Conclusion: A total of 104 patients were enrolled, with mean age 35.93 years. Males were more commonly involved compared to females. The culture results were positive among 55 patients and negative in 49 patients. The most common causative agent isolated was dermatophyte moulds followed by non-dermatophytes and yeasts.

Keywords: Onychomycosis, Distal Lateral Subungal Onychomycosis, Trichophyton Rubrum, KOH Mount, Fungal Culture and Pattern of Drug Resistance.

INTRODUCTION

Onychomycosis is a fungal infection of the toenails or fingernails that may involve any component of the nail unit, including the matrix, bed, or plate. Onychomycosis is caused by dermatophyte fungi, nondermatophyte moulds and yeasts.[1]

Onychomycosis (OM) is one of the commonest nail conditions encountered in dermatological practice. Prevalence rates for OM varying from 3 to 5% have been found in most studies; however, a few reports suggest a higher prevalence of even up to 26% in the general population.[2]

Onychomycosis has 5 main subtypes these are: Distal and lateral subungual onychomycosis (DLSO) (Fig 1), White Superficial onychomycosis (WSO) (Fig 2) (white or black): Patchy, Proximal subungal onychomycosis (PSO), Endonyx (Fig 3) and total dystrophic onychomycosis. Distal lateral subungal onychomycosis is the most common caused by Trichophyton rubrum. White superficial onychomycosis is second most common caused by Trichophyton mentagrophytes. The Proximal subungal form of onychomycosis is characteristically seen with immunodeficient people and peripheral vascular compromise.[3]

Among the dermatophytes, the most common organism reported is Trichophyton rubrum (53% cases) followed by T. mentagrophyte var interdigitale (13%), Epidermophyton floccossum (1.2%) (Fig 5) and Microsporum species.[2]

The non-dermatophyte Yeasts – Candida albicans, Candida parapsilosis and moulds -Scopulariopsis spp, Fusarium spp, Aspergillus spp, Scytalidium hyalinum.[3]

Hence through this study an attempt was made to identify the various clinical patterns of onychomycosis and to identify pattern of drug resistance in onychomycosis.

MATERIAL AND METHODS

The proposed study was carried out in Outpatient Department of Dermatology Venereology and Leprosy, Rohilkhand Medical College and Hospital, Bareilly, a tertiary care hospital in western Uttar Pradesh for one year (November 2017- October 2018). The study was explained to the eligible participants. Informed consent was taken prior to the inclusion in the study.

Inclusion Criteria:

1. Patients showing nail changes suggestive of onychomycosis namely onycholysis, onychodystrophy, subungual hyperkeratosis, discolouration of the nail plate –melanonychia or leukonychia, thickening of the nail plate and other changes.
2. Patients with the aforementioned nail changes, which are positive for fungi on direct microscopy using potassium hydroxide.

Exclusion Criteria

1. Nail clippings negative on direct microscopy
2. Patients who have received antifungal treatment for the

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past one month.

During the clinical examination specimen collection was done. All samples were identified with the relevant hospital details and sent to the microbiology laboratory for necessary tests as mentioned below.

Clinical examination

Nail Examination: Inspection of the nail plate, nail bed, lateral and proximal nail fold was done. The following clinical details were noted-discolouration of the nail plate, distal and proximal separation of the nail plate from the nail bed, thickening of the proximal and lateral nail fold, crumbling of the nail plate and subungual debri.

Specimen collection

The first step of sample collection process is thorough cleansing of the nail area with alcohol to remove the contaminants.

Nail scrapings and nail clippings were subjected to mycological study by direct microscopy using potassium hydroxide.

The samples were received by the microbiology department and subjected to digestion using 20% KOH or KOH Calcofluor supplementation. The digested material was observed under direct microscopy for evidence of fungal filaments. The culture medium SDA (Fig 4) with chloramphenicol was used.

Sensitivity to different drugs- Terbinafine, Fluconazole, Itraconazole and Griseofulvine (Table 1)

STATISTICAL ANALYSIS

The analysis of data was descriptive using SPSS version 17.0(SPSS Inc, Chicago, IL). Chi-square test was the statistical method used for analysis of the data.

RESULTS

Age distribution: A total of 104 patients were enrolled in the study. The mean age was 35.93 years. Age ranged between 14 to 72 years.

Gender distribution: Among the 104 patients enrolled, 64(62%) were males and 40(38%) were females.

	Drugs Sensitive (%)	Resistance (%)
Terbinafine	44(80)	11(20)
Fluconazole (Fig 6)	37(67)	18(33)
Itraconazole	32(58)	23(42)
Griseofulvine	28(51)	27(49)

Table-1: Drug resistance and sensitivity

Figure-1: Distal and Lateral subungual onychomycosis.

Figure-2: White superficial onychomycosis

Figure-3: Endonyx Onychomycosis

Figure-4: SDA Agar with Candida growth

Figure-5: Epidermophyton floccosum on SDA

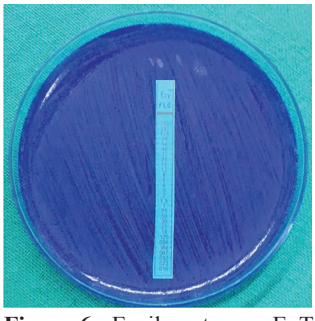

Figure-6: Epsilometer or E Test for Fluconazole (Fluconazole resistance)

Finger nail distribution: In the upper limb the thumb finger (40%) was predominantly involved followed by index finger (26%), middle finger (18%), ring finger (14%) and little finger (06%).

Toe nail distribution: In the lower limb the great toe (46%) was frequently involved followed by second toe (28%), third toe (11%), little toe (08%) and fourth toe (08%).

Finger nail and toenail distribution: Among the male patients 34.37% had finger nail involvement, 62.5% had toe nail involvement and3% had both finger and toenail involvement. In males a higher incidence of toe nail involvement was seen.

Among the female patients 70% had fingernail involvement, 20% had toenail involvement and 10% had both finger and toenail involvement. In females a higher incidence of fingernail involvement was seen.

Clinical pattern: The most common clinical pattern of onychomycosis observed was DLSO (57%), followed by TDO, MO, PO, and EO.

Fungal culture results: Among the 104 patients included in the study 55 were culture positive and 49 were culture negative.

Distribution of organisms isolated: Among the 55 culture positive Dermatophyte moulds (64%) was the most common isolate, non dermatophyte (24%) and yeast (12%).

Organisms isolated: Among the 55 organisms isolated T. rubrum (34%) most commonly isolated followed by T. mentagrophytes, Aspergillus spp., Candida spp, Floccose and Fusarium spp.

Clinical pattern of OM observed in males and females: The most common pattern of OM observed in males was DLSO followed by, MO, TDO, PO and EO. In females the most common pattern of OM observed was DLSO followed by TDO, MO, EO and PO.

DISCUSSION

Onychomycosis is a fungal infection of the nails, mainly caused by dermatophytes, but non dermatophyte moulds and yeast do play a major role in its etiology. The aim of the study was to identify the different clinical presentations of onychomycosis with respective causative agents and to find if any correlation existed between the above two groups and pattern of drug resistance.

Demographic distribution

Most of the patients in the study group (n=104) belonged to the age group ≤ 30 (49%) years with a mean age of 35.93years. This is in accordance with reports by Khosravi et al and Bokhari et al.[4,5] The higher prevalence in this age group is possibly accorded to occupation-related trauma. In this study, males (64%) were found to be more commonly affected than females (40%). The higher incidence of OM in males may be attributed to more exposure to outdoor physical activity which makes the nail prone to trauma. This finding is in agreement with Perea et al who also reported a higher incidence in males as compared to females.[6]

Fingernail and toenail distribution

The female patients were found to have predominant finger nail involvement (70%) which again could be ascribed to their frequent involvement in household work.

The males on the other hand were observed to have predominant toe nail involvement (62.5%) possibly due to a higher use of closed footwear.

In the study finger nail OM (50) was hence found to be more common compared to Toe nail (48) involvement. This appears to be in consonance with previous studies.

Among the toe nails the great toe was most commonly involved, possibly due to its greater size predisposing to more frequent trauma, as observed by other authors[7] who also reported similar findings. The thumb was more frequently involved among the finger nails probably due to an increased incidence of occupation related trauma and household work as also reported by Zaini et al.[8]

Distribution of risk factors in onychomycosis

A coexisting superficial fungal infection was observed among seven patients, majority of whom had tinea pedis. T. rubrum was most commonly isolated in this group which is in accordance with previous studies.[9]

The use of occlusive footwear was found in 17 patients. The most common clinical pattern of OM seen in this group was DLSO (13), TDO (2) and MO (2) patients.

The organisms isolated were T. rubum, T. mentagrophytes, Aspergillus spp, Candida albicans, Floccose and Fusarium spp.

However, these results were not found to be statistically significant. In comparison the use of open footwear was seen among 41 patients. The most common organisms isolated in this group were NDM species (14) followed by dermatophytes (4) and yeast (3). The higher incidence of isolating NDM species in the above group could be attributed to the higher exposure to soil saprophytes which increase the risk of onychomycosis caused by the above species.

Fusarium spp and Candida spp were the organisms isolated among two patients in whom gardening was a hobby. Such activity exposes the nail to numerous saprophytic fungi, which increases the chances of OM especially caused by NDM.

Distribution of the organism causing onychomycosis

In literature the most common causative agent isolated from onychomycosis are dermatophytes. In India, the isolation rates of dermatophytes varies from 70% to 82.35% as reported by Patwardhan et al and Adhikari et al in Aurangabad and Sikkim respectively.[10,11] Garg et al in Bhopal and Sharma et al in Shimla noted a prevalence of 23% and 32.6% respectively.[12,13]

The most common organism isolated in this study were non-dermatophyte moulds with a prevalence rate of 35%.

According to English et al, criteria used to define non dermatophyte moulds as A primary pathogen requires: (1) Isolation of NDM in pure culture (2) absence of dermatophytes and (c) demonstration of KOH positive filaments.[14] Using the above criteria, 35 of the NDM isolated in our study would qualify as primary pathogens.

Similar results have been reported by Garg et al (39%) and Ramani et al (22%) respectively.[12,15] In comparison, Patwardhan et al isolated (13.6%) and Yenisehirli (3.3%) non dermatophytes, respectively.[10,16] In this study OM caused by non-dermatophyte moulds were more frequently affecting toenails (19), probably since non-dermatophyte moulds are

often present in soil. Among the non dermatophytic moulds Aspergillus species was isolated among 15% cases followed by Fusarium species in 15%, Cladosporium species 2%, Scytalidium species 2% and mixed infection in 1%. Similar results were noted by Garg et al wherein, Aspergillus species was isolated among 9% cases followed by Fusarium species in 5%.[12] However other non-dermatophytes like Penicillium, Acremonium and Zygomycetes species were not isolated in our study. In our study among the nondermatophytes Aspergillus species were isolated commonly from DLSO (10%) cases followed by, TDO (2%), MO (2%) and SO (1%). Among the 15% patients affected by Fusarium species; 4% showed a thickening of the proximal nail fold, a feature of infection with the above species.[17]

In comparison, T. verrucosum and T mentagrophytes have been rarely isolated as a causative agent of onychomycosis. Garg et al isolated T verrucosum among 2% of the patients who had incidental exposure to cattle.[12]

Yeasts have been identified as the sole etiologic agents of onychomycosis. Candida albicans was isolated from 6% cases, especially from the fingernails in females (4/6patients). The predisposing factors appear to be working environment (e.g. kitchen or laundry work) and the hot humid climate. In Lahore, Pakistan Candida was the most common pathogen isolated from fingernails in females.[5] The reason could be attributed to ritualistic washing of hands and feet and climatic factors as mentioned above. In our study Candida species was commonly isolated in DLSO (3%) followed by, CP (1%) MO (1%) and TDO (1%). This result is in concordance with Gupta et al where Candida species was isolated from DLSO (2%) patients.[12]

Distribution of the clinical pattern of onychomycosis

The most common pattern of onychomycosis seen was DLSO 59(70%) followed by TDO 13 (11%) mixed 17 (11%), PO 11 (6%) and EO 4 (1%). This finding is in accordance with reports by Garg et al and Patwardhan et al.[12,10] PO was not associated with any immunodeficiency disease in contrast with previous reports[18] but consistent with Bokhari et al.[5] The clinical patterns DLSO, TDO, MO and PO were seen affecting both fingernails and toenails; while SO affected only fingernails. Similar results were noted by Bokhari et al.[5] However no cases of endonyx onychomycosis was seen in our study.

CONCLUSION

The clinico-etiologic correlation revealed that a single pathogen could give rise to more than one clinical type of onychomycosis and, a given clinical pattern of onychomycosis can be caused by various organisms. Therefore, it is not possible to identify the causative fungus by merely examining the diseased nail. Pattern of drug resistance maximum is of Griseofulvin (49%) and least is of Terbinafine (20%).

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