

## Dermatophytosis in One-Health Perspective

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### ABSTRACT

Dermatophytosis is associated with a unique group of fungi commonly known as dermatophytes and usually infect keratinous tissue, stratum corneum of the skin, invade the hair, nails of the host, feathers, horns and hooves. It is a contagious cutaneous infection usually prefer a hot and humid environment for their growth and infectivity, therefore, commonly occur in tropical regions worldwide. Phylogenetically, dermatophytes are closely related to monophyletic keratinophilic filamentous fungi. These are categorized into three genera i.e., Epidermophyton, Microsporum and Trichophyton. Dermatophytosis is commonly named after the body part get infected with the dermatophytes i.e., T. capitis if scalp and hair are involved, T. unguium if nails are affected, T. corporis if non-hairy skin become affected etc. Most of the dermatophytes resides in soil for years hence named geophilic. The dermatophytes adapted to humans are called anthropophilic, whereas some dermatophytes are adapted to animals known as zoophilic. Both geophilic and zoophilic are capable to transmit to the humans directly through arthroconidia shed by infected skin and/or hair of the infected host and deposited on fomites such as brushes and clippers. Dermatophytosis (tinea capitis) is more common in children (up to 60%), while tinea pedis is prevalent more than 50% in adults. Tinea cruris is more common in population lives in hot climates. Mostly, dermatophytosis can be serious in immunosuppressed individuals. The infection usually resolves within 2-4 weeks with topical application of the drugs like eficonazole and tavaborole and/or oral administration of the drugs i.e., itraconazole, fluconazole, griseofulvin, terbinafine etc. In order to control dermatophytosis effectively, One-Health approach highlights the significance of cooperation between medical professionals, veterinarians, environmental scientists, and public health specialists.

**Keywords:** Dermatophytes, Skin infection, Zoonosis, One-Health approach, Prevention

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## 1. INTRODUCTION

Dermatophytosis is a common contagious mycotic infection associated with a mold group of fungi known as dermatophytes and cause cutaneous infection (Chanyachailert et al. 2023). Dermatophytes are unique group of fungi and possess alike antigenicity, infectivity and usually prefer a hot and humid environment for their growth; therefore, dermatophytosis commonly occur in tropical regions. Dermatophytes infect keratinous tissue and are able to break keratin in tissues and invade the hair, the stratum corneum of skin, nails of a living host, feathers, horns and hooves (Tachibana et al. 2017; Jartarkar et al. 2020). Dermatophytes are usually classified on the basis of the body parts they affect and referred to as ringworm or tinea derived from Latin word for “larva” or “worm” i.e., *Tinea capitis* (*T. capitis*) if dermatophytes affect scalp and hair, *T. corporis* if affect non-hairy skin, *T. unguium* if affect nails, also called onychomycosis, *T. manuum* if dermatophytes involved hands, *T. cruris* if involved groin, *T. pedis* if feet are involved etc. (AL-Khikani 2020; Jartarkar et al. 2020). Most of the dermatophytes reside in soil (geophilic) for years. Some dermatophytes are adapted to humans (anthropophilic), whereas few are adapted to animals (zoophilic). The zoophilic and geophilic are capable to transmit to the humans and are of zoonotic importance (Jartarkar et al. 2020; Chanyachailert et al. 2023). Dermatophytes usually remain in stratum corneum of the skin, thereby can be self-limiting disease. In livestock, it is of economic importance because it damages the hides (Chanyachailert et al. 2023).

## 2. ETIOLOGY

Phylogenetically, dermatophytes are closely related to monophylectic keratinophilic filamentous fungi. These are categorized into three genera i.e., *Epidermophyton*, *Microsporum* and *Trichophyton*. The species of these genera which cannot invade and infect keratinous tissue are not included in the dermatophytes. The life cycle of the dermatophytes usually has two phases: the anamorph state (also known as imperfect state) which is the asexual phase, and the teleomorph state (also known as perfect state) that is the sexual phase. Although the teleomorphs state has not yet been identified but the generic name given to the dermatophytes that accommodates the known sexual forms is *Arthroderma* and refers to both *Microsporum* and *Trichophyton* (Ghannoum and Nancy 2009; Smith and McGinnis 2011; Jartarkar et al. 2020).

## 3. EPIDEMIOLOGY

### 3.1. CLASSIFICATION

Dermatophytes are also classified as under on the basis of principal ecologic niches as (Moskaluk and VandeWoude 2022);

- Anthropophilic commonly named as human loving
- Zoophilic also known as animal loving
- Geophilic commonly known as soil loving

It is worth mention here that many dermatophytes possess characteristics of two or more ecological niche. This classification helps to determine the source of infection caused by dermatophyte. Among these three niches, zoophilic and geophilic dermatophytes are of clinical importance and causes severe inflammation with self-limiting lesions. However, anthropophilic dermatophytes cause less inflammation but chronic lesions (Segal and Elad 2021; Chanyachailert et al. 2023).

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### 3.2. TRANSMISSION

Dermatophytes infect humans and animals after contact with spores (conidia) growing in a vertebrate host normally form only arthrospores (arthroconidia). The dermatophytes are usually transmitted directly through arthroconidia shed by infected skin and/or hair. These infected hyphal fragments and arthroconidia can easily disseminate from infected host and deposited on fomites such as brushes and clippers and transmitted to the others. Some studies had reported that these arthroconidia are the primary cause of new infections and remain viable in the environment for several years (Smith and McGinnis 2011; Segal and Elad 2021).

### 3.3. GEOGRAPHICAL DISTRIBUTION

Distribution of dermatophytes is worldwide with variability to the individual species. As the hot and humid environment favors the growth of dermatophytes, therefore, these are more prevalent in tropical and subtropical regions. The prevalence of the species in a geographic zone is dependent on certain factors i.e., migration pattern of the population, primary and secondary host range, lifestyle standards and climate preferences. Some species are restricted to a particular geographic zone, e.g., *Trichophyton concentricum* (*T. concentricum*) is endemic to the South Pacific and some area of South America and not reported in Europe (Ghannoum and Nancy 2009). Contrarily, *Microsporum canis* (*M. canis*), *T. tonsurans* and *T. violaceum* are common in Europe, Middle East and Africa (Farang et al. 2018; Chanyachailert et al. 2023). Whereas prevalence of *M. canis*, *M. nanum*, *T. verrucosum*, *T. mentagrophytes*, *M. gypseum* and *T. equinum* is established worldwide. In Asia especially Indian Subcontinent, *T. simii* is thought to be endemic (Beguin et al. 2013; Farang et al. 2018; Segal and Elad 2021).

Dermatophytosis occurs at different sites of the body. Many scientific reports are published in this regard which indicate the occurrence of dermatophytosis at different sites and parts of the body. Dermatophytosis is the infection caused by a dermatophyte but it is observed that all dermatophytes are not involved in causing the infection. The dermatophyte (fungus) colonizes in the stratum corneum of the skin but it does not penetrate the viable tissues because it grows in a radial manner in the stratum corneum (Sultan et al. 2020; Martinez-Rossi et al. 2021). Invasion of the dermatophyte into the hair is an example of colonization of the dermatophytes in the non-living tissue. The colonization of the fungus in the stratum corneum may result in the development of the disease. Infection of the skin and other body parts also depend on the region. In Africa, tinea capitis is common which is also called as with a prevalence of 14-86% in children (Farang et al. 2018). Reports based on the data of two-decades have shown that *Trichophyton tonsurans* is the major causative agent that infect children with tinea capitis and achieved near exclusionary proportions in the USA (Sultan et al. 2020; Segal and Elad 2021; Chanyachailert et al. 2023). Similarly, the same dermatophyte infects the scalp and hair of the children in Canada (Petrucci et al. 2020; Chanyachailert et al. 2023). Whereas *T. violaceum* is a major causative agent associated with tinea capitis in the children of India and Nepal (Beguin et al. 2013). Prevalence of dermatophytosis of the skin is higher in tropical regions (Andrews and Burns 2008; Smith and McGinnis 2011). The rate of infection is higher in non-natives to that of the indigenous population. It is essential to study different genera of the dermatophytes, their management, prevention and control of infection to understand the epidemiology of dermatophytosis (Martinez-Rossi et al. 2021).

### 3.4. MORBIDITY AND MORTALITY

It is observed that exposure of individuals to the spores of dermatophytes does not always lead to the infection. However, prevalence of dermatophyte infections varies with risk factors like the

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climate, skin injuries, hot and humid environment and the animal contact because dermatophytosis is a common disease of puppies and kittens, however, there is no evidence of increased risk of the infection in elderly pets (Moriello 2019). Dermatophytosis (tinea capitis) is more common in children (up to 60%), while tinea pedis is prevalent more than 50% in adults. Tinea cruris is more common in population lives in hot climates. Mostly, dermatophytosis is not serious in healthy individuals; however, it can be serious in immunosuppressed individuals. The infection usually resolves within 2-4 weeks with good treatment (Andrews and Burns 2008; Smith and McGinnis 2011; Martinez-Rossi et al. 2021).

### 4. CLINICAL MANIFESTATIONS AND TREATMENT

Clinical manifestations of the dermatophytosis depend on the involvement of body area. The term tinea (Latin word for “larva” or “worm”) is used to describe the area of body involved. The most common body sites infected with dermatophytosis are termed as: *T. capitis* (scalp and hair), *T. corporis* (non-hairy skin), *T. unguium* (nails, also called onychomycosis), *T. manuum* (hand), *T. cruris* (groin), *T. pedis* (feet) etc. (Ghannoum and Nancy 2009; Smith and McGinnis 2011; Martinez-Rossi et al. 2021). Below are the clinical manifestations of some of the most common types of dermatophytosis:

#### 4.1. TINEA CAPITIS

##### 4.1.1. SYNONYMS

Tinea tonsurans, Ringworm of the eyebrows, eyelashes and scalp

Tinea capitis is the common disease primarily found in the infants, children and young adolescents all over the world (Andrews and Burns 2008) which involve infection of the hair shaft and scalp. It causes stratum corneum’s scaling associated with inflammation and sometime inflammation may not be there. It may be one of the two types of infection: ectothrix or endothrix. In ectothrix, the arthroconidia of the dermatophytes cover the surface of hair shaft and could be easily recognized by the destruction of hair follicle, while in endothrix, hyphae form arthrospores within the hair shaft. Invasion of dermatophytes in scalp hair follicles results in alopecia. The causative agents for this form of dermatophytosis (tinea capitis) is either *Microsporum* or *Trichophyton*. *M. canis* and *M. audouinii* are the species which cause pronounced inflammatory response and is of ectothrix type, whereas *T. tonsurans* invades in the hair shaft and causes endothrix type of infection (Ghannoum and Nancy 2009; Smith and McGinnis 2011; Seema et al. 2017). This disease usually spread from humans to humans (anthropophilic), however it is also transmitted from soil to the humans (geophilic) and from animal to humans (zoophilic) (Petrucci et al. 2020).

Tinea capitis occurs on eyebrows, eyelashes and scalp. At early stages, lesions are present in the form of papules, pustules or nodules with alopecia. As disease progresses, itching becomes intense and there is development of erythematous papules or kerion on the scalp. Kerion is an inflammatory pus-filled folliculitis. Kerion is different form favus (Latin word means “honeycomb”). Favus is a special form of endothrix in which a crust is formed along the hair shaft due to accumulation of pus of hair follicle which looks like crusted-honeycomb (also termed as scutula) on the scalp and lead to hair loss. Favus is associated with *T. schoenleinii*. Dermatophytes of two endothrix species *T. tonsurans* and *T. violaceum* tend to induce severe and chronic infection than those of ectothrix and causes “black-dot ringworm” that is characterized by a “black-dot” on the scalp due to breakage of infected hair (Smith and McGinnis 2011; Gupta and Drummond-Main 2013; Seema et al. 2017).

The treatment regimen for tinea capitis is as follow (Gupta and Drummond-Main, 2013):

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- Oral administration of the antifungal agents is recommended for eradication of fungal infection present in hair or hair follicles. For that, Griseofulvin is used @ 10 mg/kg/day continuous for 10 weeks (Gupta and Drummond-Main 2013).
- For reduction of treatment periods, itraconazole @ 5 mg/kg/day is recommended for continuous up to 4 weeks.
- Another effective antifungal agent fluconazole is used @ 3-6 mg/kg/day for 6 weeks.
- Terbinafine is considered more effective and can be recommended for 4 weeks at the dose rate as follow:
  - The children weigh <20 kg is 62.5 mg/day
  - Patients weigh 20-40 kg @ 125 mg/day
  - Adults weigh >40 kg @ 250 mg/day
- To reduce the risk of disease progression, topical treatment should be applied along with oral therapy. For that purpose, creams and shampoos can be used which contain azoles and selenium sulfide (Seema et al. 2017).

### 4.2. TINEA CORPORIS

#### 4.2.1. SYNONYM

Ringworm of the body

Tinea corporis refers to the colonization of arthroconidia of dermatophytes on glabrous skin. It is superficial fungal infection and limit itself in the superficial layer radially without involving the viable tissues. It excludes the hand, feet, face, scalp, nails and groin region. All species of *Epidermatophyton*, *Trichophyton* and *Microsporum* are able to produce lesions of tinea corporis, however, most prevalent etiological species are *M. canis*, *T. rubrum* and *T. mentagrophytes*. Lesions produced by these species are ring-shaped and may be single, multiple or confluent. The fungus invades and colonize in the stratum corneum for 1-3 weeks. After colonization, it exhibits two basic types of lesions as clinical signs i.e., annular and vesicular. Lesions show inflammatory responses from low range causing small, dry scaling and erythematic annular patches to a high inflammatory lesions (vesicular type) like vesicles, pustules and marked erythema with subsequent crust formation. Zoophilic dermatophytes such as *T. mentagrophytes* usually exhibit the characteristic of vesicular lesions. Infection of hair follicles can lead to pustular, reddened, psoriasiform plaques, elevated or verrucous lesions with a severe inflammatory response as exhibited by kerion is termed Majocchi's granuloma (Smith and McGinnis 2011; Seema et al. 2017; Martinez-Rossi et al. 2021). Due to this severe inflammatory lesions, secondary bacterial infection may occur due to involvement of opportunistic bacteria. A special form of *T. corporis* named *T. imbricata* that is reported in the population of Southeast Asia, South America and Pacific Islands of Oceania. This form is associated with *T. concentricum*. The lesions of this disease spread over 70% of the body and characterized by polycyclic rings of papulo-squamous scales. Transmission of this disease is through direct contact and genetic susceptibility inheritance in an autosomal recessive pattern is also reported (Ghannoum and Nancy 2009; Smith and McGinnis 2011).

Therapeutic regimen recommended for the treatment of tinea corporis is as under (Ghannoum and Nancy 2009; Smith and McGinnis 2011):

- Topical application of creams contains antifungals agents like ketoconazole, econazole, terbinafine and clotrimazole for drying the involved skin.
- For oral treatment, any antifungal drug from the following can be used:
  - Griseofulvin @ 500 mg/day continuous for up to 6 weeks
  - Itraconazole @ 100 mg/day for 2 weeks

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- Fluconazole @ 150 mg/day continuous for 6 weeks
- Terbinafine @ 250 mg/day continuous for 4 weeks

### 4.3. TINEA UNGUIUM

#### 4.3.1. SYNONYMS

Nail's Ringworm, Onychomycosis, Dermatophytic onychomycosis

Fungal infection of nail is called tinea unguium associated with dermatophytes. The other term which makes a confusion is onychomycosis which refers to infection caused by any non-dermatophytic fungus. However, onychomycosis is the term that commonly used to describe all fungal infections of the nail. In this chapter, we will discuss onychomycosis due to dermatophytes. The prevalence of onychomycosis is 2-13% of the general population. The prerequisites of this condition are already existence of the tinea pedis in the same individual, immunosuppression, age, hot and humid environment and genetic predisposition. Onychomycosis occurs after invasion of the dermatophytes into the nail. It starts from the lateral distal subungual surface of the nail associated with *T. rubrum* and sporadically by *T. tonsurans*, *T. mentagrophytes* or *E. floccosum*. The condition is characterized by white, crumbly appearance of the nail due to accumulation of crumbling subungual debris, the nail become thickened due to subungual hyperkeratosis. The superficial white nail appears due to white patches on the nail's surface and is associated with *T. mentagrophytes*. Severe cases involve entire nail surface which causes dystrophy of the nails and involves the cornified layer of the nail bed and hyponychium (Ghannoum and Nancy 2009; Smith and McGinnis 2011).

The success of treatment depends on identification of the causative agent.

- Topical application of creams containing antifungal agents has low success rate because of poor penetration. However, new agents eficonazole and tavorole are known for good penetration in the nail and are more effective than older agents (Jinna and Finch 2015; Tachibana et al. 2017).
- Oral administration of antifungal agents is recommended for the treatment of tinea unguium. Following agents can be used:
  - Itraconazole @ 400 mg/kg daily for a week. Must be repeated after a month and continued for 3-4 months for toenail involvement.
  - Fluconazole @ 150-300 mg once a week for 6-12 months. Treatment may be continued till normal growth replace the infected nail
  - Terbinafine is given @ 250 mg/day daily for 5-6 weeks for fingernails and 10-12 weeks for toenails. Meta-analysis of the worldwide published data reported that terbinafine has more success rate than other agents (Gupta et al. 2013).

### 4.4. TINEA PEDIS

#### 4.4.1. SYNONYMS

Foot Ringworm, Athlete's foot

Tinea pedis or foot ringworm is the term designated for dermatophytosis of the feet. It is thought to be the most common dermatophytosis with prevalence rate of 30-70%. The typical sites of infection are interdigital spaces and soles. If infection involves entire foot, then the term used is moccasin foot. The infection varies from mild to severe, acute to chronic and may have inflammation, vesicles and pustules (Canavan and Elewski 2015; Turkistani et al. 2022). Predisposing factors of the infection are hot and

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humid environment, age, gender (common in males than females), absence of sebaceous glands in feet, wearing of shoes. The most common clinical form of *T. pedis* is interdigital clefts of the toe and characterized by maceration, shedding, and fissuring of the skin having dead skin (white epidermis) and odor. It may spread to the sole, heel and dorsal surface of the foot. The principal etiologic agents of *T. pedis* are *T. rubrum* and *T. mentagrophytes var. interdigitale*. It is thought that if *T. pedis* remained untreated the it may lead to onychomycosis (Canavan and Elewski 2015; Turkistani et al. 2022). The infection caused by *T. mentagrophytes var. interdigitale* exhibits vesicular form of the disease in which ulcerative eczematoid vesiculo-pustules or bullae occurs which spread to the heel, anterior area and dorsal surface of the foot. Involvement of opportunistic bacteria exaggerates the condition and lead to cellulitis, lymphangitis and lymphadenitis (Canavan and Elewski 2015; Jartarkar et al. 2020; Turkistani et al. 2022).

Tinea pedis is successfully treated with combination of topical and oral antifungal agents. Following regimens are recommended for the treatment (Subissi et al. 2010; Scorzoni et al. 2017):

- For topical application, preparation of luliconazole, benzylamine, ciclopirox olamine, haloprogin, and naftifine 2% is recommended for 1-2 weeks.
- Oral administration of itraconazole @ 400 mg/kg daily for one week.

### 5. NEW AGENTS FOR THE TREATMENT OF DERMATOPHYTOSIS

Following are the new agents discovered by the scientists for the treatment of dermatophytosis and must be checked in humans:

- Apigenin, a flavone, has shown effective against certain dermatophytes in mice and should be tested in humans (Singh et al. 2014).
- Tavaborole is a broad spectrum oxaborole which showed effective in humans against certain dermatophytes (Elewski 2014).

### 6. DIAGNOSIS

There are three major methods for diagnosis of dermatophytosis (Aboul-Ella et al. 2020; Moskaluk and VandeWoude 2022; Chanyachailert et al. 2023).

#### 6.1. CLINICAL EXAMINATION

The suspected case of fungus can be initially screen out by using Wood's light (filtered ultraviolet light). Under this light, hair or skin infected with *Microsporum* will exhibits a bright blue-green fluorescence which will help to go for further examination of that animal (Aboul-Ella et al. 2020; Moskaluk and VandeWoude 2022; Chanyachailert et al. 2023).

#### 6.2. LABORATORY EXAMINATION

In this method, clinical sample of skin is added to 10% potassium hydroxide (KOH). A drop of that sample is then placed on glass slide and covered with a cover slip. After 3 minutes of preparation of glass slide to allow for digestion of host cells, it is examined under microscope at 400x under phase-contrast microscopy. We can observe the presence of septate hyphae or fungal conidia under phase contrast microscopy. This procedure will confirm the presence of fungal disease in that sample (Aboul-Ella et al. 2020; Moskaluk and VandeWoude 2022; Chanyachailert et al. 2023).

## 6.3. CULTURE METHOD

For identification of species of the fungus, sample should be cultured on selective, such as Mycosel and Mycobiotic agar, and non-selective fungal media, such as Sabouraud dextrose agar and potato dextrose agar. These cultures are recommended to grow in Petri plates sealed with gas-permeable tape or parafilm or screw-capped tubes. These cultures for dermatophyte isolation should be then incubated at 30°C for 1-2 weeks before examination (Aboul-Ella et al. 2020; Moskaluk and VandeWoude 2022; Chanyachailert et al. 2023).

## 7. PREVENTION AND CONTROL

Prevention and control of the disease is possible by adopting following measures (Jartarkar et al. 2020; Chanyachailert et al. 2023):

- One of the major preventions is to control the disease in animals to avoid human dermatophytosis caused by zoophilic.
- Animals suffering from dermatophytosis should be kept isolated and properly treated. Other animals of that area should be examined with Wood's light.
- Area and fomites of the affected animal must be disinfection properly and remnants (hair, wool, nails etc.) of the diseased animal should be disposed.
- Vaccine should be developed and used for prevention and control of the disease.
- Good hygiene of the individual and environment is necessary to reduce the occurrence of the disease.
- Skin should be kept clean and dry especially the feet and groin skin (Chanyachailert et al. 2023).

## 8. CONCLUSION

In summary, considering dermatophytosis from the standpoint of One Health emphasizes the intricate interactions that occur between environmental, animal, and human variables in the development and treatment of this fungal illness. Humans and animals are both impacted by the frequent dermatological illness known as "dermatophytosis," which highlights the connection between animal and human health. In order to effectively treat dermatophytosis, this One Health approach highlights the significance of cooperation between medical professionals, veterinarians, environmental scientists, and public health specialists. Through comprehending the common risk factors, pathways of transmission, and reservoirs associated with this fungus, we may create more potent preventive and management plans

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