Review Article

Dermatophytosis a Worldwide Contiguous Fungal Infection: Growing Challenge and Few Solutions

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Abstract

Dermatophytes are filamentous fungi that survive on keratinous materials. There is a broad prevalence of dermatophytes infection among the world. Dermatophytosis is the disease that mainly caused by different species of dermatophytes within the cutaneous layer of the skin. It has contagious properties to spread from person to another and also from the animal to the human. The skin, hair, and nail of all types of mammalian, including human, are under the risk to develop dermatophytosis. A total of 2530 articles have been investigated in PubMed ($n = 1525$), Medline ($n = 705$), and Google Scholar ($n = 300$). From 2530 articles, just 48 studies were included in this review. This study aimed to review available data and current literature as well as information from personal experiments regarding dermatophytes infection to focus on the dermatophytes general features, dermatophytosis, pathogenesis presented by enzymes production, most common factors associated with infection, prevalence, and treatment of dermatophytes infection, and also to yield a clear vision to other researches about this worldwide predominant contiguous fungal disease.

Keywords: Cutaneous infection, dermatophytes, dermatophytes infection, dermatophytes treatment, dermatophytosis

Introduction

Dermatophytosis or tinea is a predominance in about 20%–25% of all total world populations.[1,2] Dermatophytes are filamentous fungi naturally living on keratinous materials found in soil.[3] Dermatophytosis or tinea is mainly caused by dermatophytes.[4] Dermatophytosis or tinea can be found on the skin of different parts of the human body which make it takes various names based on the infected area such as tinea pedis on the feet, tinea unguium on the nails, tinea capitis on the scalp, tinea cruris on the groin, and tinea corporis on the body.[5] It is considered prevalent skin disease worldwide.[6] Moisture and warm conditions are the most suitable factors to a wide distribution of dermatophytosis in tropical countries.[1] This epidemiological distribution may change with migration, lifestyle, immunosuppressive state, drug therapy, and socioeconomic conditions.[1,7] The treatment of dermatophytosis needs about 2–4 weeks to be cured in many types and may require many months in cases of tinea capitis and onychomycosis.[8]

General Features of Dermatophytes

Dermatophytes contain three genera, including *Trichophyton* spp., *Microsporum* spp., and *Epidermophyton* spp.[9,10] They also can divided into three groups based on the source of infection. The first one is anthropophilic when infection transmitted from human to another through the direct contact,[10] as with Microsporum langeronii which found it caused tinea corporis in most children of a public primary school of Antananarivo (Madagascar)[11] and *Trichophyton interdigitale* is a causative agent of tinea faciei.[12] Zoophilic is another group of dermatophytes when the fungi transmitted from animals, domestic or wild, to human or other animals[10] as with *Microsporum canis* and *Trichophyton mentagrophytes* which commonly infect dogs and cats in Italy.[13] The third group of dermatophytes is geophilic which found in soil living on keratinous materials as saprophytes and can transmit to humans after contact with contaminated soil as with *Microsporum gypseum*.[10] The infection by an anthropophilic

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type of dermatophytes usually recognized by the chronic nature with low inflammation while inflammation is high when the disease caused by zoophilic or geophilic.[14]

Dermatophytes are a special group of keratinous fungi which have the ability to live on keratin-rich materials that found in soil or the human or animals tissues such as the skin, hair, and nail.[3]

The phylogeny of dermatophytes is more influenced by the environmental location of these fungi. Sexual reproduction is very clearly observed among a geophilic group and some of zoophilic, while it rare observed among the anthropophilic group.[15]

Dermatophytosis

Dermatophytes have the ability to cause a cutaneous skin disease called dermatophytosis. This disease considers a common fungal infection in different parts of the human body which enrichment with keratin, especial hair, skin, and nail.[10] It is also called ringworm when the lesion appears as a ring shape with a clear center and inflammatory edge.[9,10] Tinea is the another term of dermatophytosis which could take a different name based on the infected site of the human body such as tinea unguium (onychomycosis) in fingernails, tinea faciei on the face, tinea pedis (athlete's foot) on the feet, and tinea corporis on any glabrous skin.[10,14] Infection usually occurs in both genders at different ages [Figure 1].[16,17]

A lesion of tinea can be caused by a single species of dermatophyte or by many species in some cases.[18] In addition, a single species of dermatophytes can cause different types of tinea.[19]

There are approximately 100,000 species of fungi from millions of species of fungi on the earth that have the ability to cause diseases for human and animals, especially in the temperate and tropical countries.[1] The general features of tinea on the infected skin of the human represented by the presence of an annular patch with an advancing, raised, scaling border, and central clearing.[5] The general clinical features of tinea on the human body are represented by the gradual appearance of the annular erythematous lesion with central healing tendency. Scaling, pustules, itching, inflammation, and hair and nail loss are also the characters of most dermatophytosis infection.[6]

Enzymes in Dermatophytes

The ability of dermatophytes to use keratin protein, the main protein constituent of hair, nails, and skin, is related to its production of a proteolytic keratinase.[10,14] However, more than 20 types of protease can produce by dermatophytes that play a role in the invasion of keratinized structure and causes infection, but the role of them as a virulence factor is not specific.[20] Other types of an enzyme can also produce by dermatophytes using for digestion processes such as alkaline phosphatase and N-acetyl-beta-glucosaminidase.[21]

The ability of dermatophytes to produce various proteins or enzymes plays an important role to invade keratinous skin layers.[22] Keratinases, adhesins, lipases, phosphatases, DNases, and nonspecific proteases are important enzymes that give the fungi the ability to attach and penetrate the stratum corneum of the skin, overcome host immune system, and scavenge nutrients.[22] Keratinase and phospholipase found to be produced by 96% of 234 clinical dermatophytes isolates, whereas gelatinase and elastase produced from 14% to 23% of isolates, respectively.[23] The acidic nature of the skin stimulates dermatophyte to produce sensing transcription factors such as PacC and Hfs1 to raise fungi adapting to this acidic pH and give them time to increase pH value after keratin degradation for elevating protease enzymes activity.[22]

Enzymes play an important role in dermatophytes pathogenesis that may be used as diagnostic tests to differentiate different species of dermatophytes, and also understanding the action of these enzymes give us crucial data to fight this fungus.

Factors Associated with Dermatophytes Infections

In addition to enzymes, several factors can associate with a high prevalence of dermatophytosis [Table 1], such as

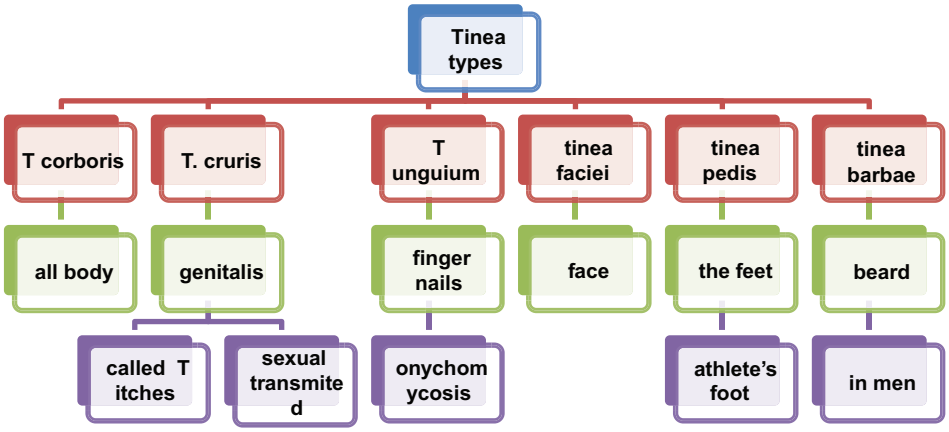

Figure 1: Tinea types with location on the body

Table 1: Risk factors associated with dermatophytosis treatment and prevalence

Risk factors	Comments	References
Short incubation period of dermatophytes	Usually from 1 to 2 weeks	[10]
Some of chronic disorders in the human body	Distribution of infection as found among patients with diabetes	[10]
Close contact with animals	Zoophilic nature of dermatophytosis	[14]
Type of geographical regions	Rural areas more susceptible to dermatophytes infection than urban regions	[16]
High temperature and humidity	Tropical and subtropical regions	[24]
Immunocompromised persons	Patients under immunosuppressive drugs and diseases such as AIDS	[25]
Long duration of treatment	Reach to 6 months in cases of tinea capitis and onychomycosis	[26]
Few antifungal drugs to treat dermatophytosis	Using of primary experiments provide promising results about the efficiency of antifungal drugs	[27]

high temperature and humidity in tropical and sub-tropical regions[24] and type of geographical regions when the infection is the most common in rural areas than in urban regions.[16] The chronic diseases or disorders in the human body are also playing a role in the distribution of infection as found among patients with diabetes.[10] Patients living in low socioeconomic conditions are highly infected by these organisms than those living in middle and high socioeconomic status, and tinea infections are significantly occurred in the developed countries due to receiving immunosuppressive drugs and diseases such as AIDS.[25] Moreover, close contact with animals, using antibiotics and steroid drugs, and also living in the community are also increased infection.[14]

The incubation period on the human skin for the development of dermatophytosis is usually from 1 to 2 weeks. Humidity and warm temperature are the most effective factors for infection development.[10]

Moisture and warm conditions are the most encouraging factors for the development of dermatophytosis in tropical countries.[1] Other factors, including the increasing sweating result from outdoor physical human activities in hot weather and low degree of hygiene, are also associated with the prevalence of dermatophytosis.[19] However, the prevalence of dermatophytosis changed due to lifestyle, traveling, socioeconomic conditions, antifungal uses, and immunosuppressive status.[1,7]

Prevalence of Dermatophytes

Dermatophytes take a different pattern of infection in worldwide, which reflect a variable geographic distribution of this disease.[7]

The investigation for these fungi is very important in the diagnosis, treatment, and differentiation from other clinical skin diseases.[28] *Trichophyton rubrum* is the predominant isolates from humans followed by *T. mentagrophytes*.[19,29-31] This is clear in Europe when a high incidence of *T. rubrum* infection was recorded, whereas *T. mentagrophytes* was a higher incidence in Asia.[1]

The prevalence of dermatophytosis differs from one country to another or even in the same country. Among 67 Iraqi patients with various dermatophytosis infections, tinea pedis (45.1%) was the most common infection, followed by tinea manuum (22.2%), tinea capitis (11.8%), tinea corporis (7.8%), tinea unguium (5.9%), and both of tinea faciei and tinea cruris (3.57%).[17] Tinea capitis showed the most clinical type of dermatophytes (1.01%) among school children in the Menoufia governorate of Egypt.[32] In Saudi Arabia, tinea corporis and tinea cruris were the most common infections in the Eastern province due to the stretched of this region along with the Arab Gulf region.[16] About 76% of 52 children of Madagascar suffering from tinea corporis and 64% from tinea capitis.[11]

A study of 5 years in Kuwait showed that *T. mentagrophytes* is the most prevalent (39%) species among 2730 patients, followed by *M. canis* (16%) and *Epidermophyton floccosum* (6.2%).[33] *T. mentagrophytes* is also revealed the highest percentage of infection (57.14%) than other species, including *T. rubrum, Trichophyton verrucosum, Trichophyton schoenleinii, Trichophyton violaceum, M. canis,* and *Microsporum audouinii*.[17]

From 115 patients with dermatophytosis in Baghdad, tinea corporis (26.7%) was the high prevalence than other types of tinea, whereas tinea manuum was the less prevalence.[34] This also recorded in India when tinea corporis (35.4%) represented the most predominant type followed by tinea cruris (16.8%) and tinea capitis (16.7%).[35]

M. canis found with a higher prevalence (50.3%) than *T. mentagrophytes* var. *mentagrophytes* (35.4%) in patients of South-east Serbia.[36] Another study performed in the same Southeast Serbia for 6 years (2012–2017) also confirmed that *M. canis* (63.9%) was the most prevalence than *T. mentagrophytes* (21.8%).[37] In Saudi Arabia, *M. canis* was the most prevalent species of dermatophytosis, and it represented 5.8% as a causative agent of tinea corporis.[38] In general, *Trichophyton* species are the most causative agents of dermatophytosis in the human, followed by *Microsporum* spp., and less by *Epidermophyton* spp.[39,40] From the *Trichophyton* genus, the *T. rubrum* is the common isolate from the dermatophytosis lesion, followed by *T. mentagrophytes*.[31,41] *T. mentagrophytes* could also be common in other studies as found when it isolated from 30 positive patients in Baghdad which represented 21.7% compared with *E. floccosum* (17.4%) and *Trichophyton bullosum* and *Trichophyton tonsurans* (13.0%).[34]

On observation from these studies, there is clearly no region clear from infection with dermatophytosis worldwide; the different incidence of dermatophytes infection is noted in neighboring countries or even in the same country with various patterns.

Dermatophytes Infection Treatment

The poor medical care will increase the epidemic spread of skin mycoses, including dermatophytosis.[42] Both systemic and topical antifungal drugs are used to treat dermatophytes infection. Different drugs are used today for the topical treatment of dermatophytosis infection. Itraconazole of azoles group and terbinafine of allylamines group are the most common type of topical treatment of dermatophytosis [Figure 2].[26]

Dermatophytosis usually needs at least 2–4 weeks to be cured in approximately all of its types and may reach to 6 months in cases of tinea capitis and onychomycosis.[8,10,26] In the recent studies, the duration time of tinea corporis was ranged from 2 weeks to 1 month. In general, superficial mycosis is usually shown a low tendency to self-limitation.[42,43]

There are always differences between the results of *in vitro* and *in vivo* exterminates. These differences may be related to either of the host conditions, such as immune response, site of infection, and underlying illness or to the fungal characters as with virulence, or the antifungal agent, such as dose, pharmacodynamics, pharmacokinetics, and drug interaction.[44] The primary experiments provide promising results about the efficiency of topical drugs against fungi and to reduce the adverse effects of intravenous usage.[27]

There are many advantages to using antifungal as a topical treatment of dermatophytosis. First, discover new drugs or modification and old one will participate to increase the available limited number of antifungal drugs.[45] Second, topical preparations are much less costly than orally administered antifungal drugs and cause minimal adverse side effects.[8,46] Third, quality of patient life will increase if new drug improved to cure infectious lesions in short time.[45]

The treatment can shorten the course of the disease to prevent spread to other animals and peoples.[43,47] Thus, a combination of different drugs may show good efficiency.[48] Long duration periods of treatment, drug resistance, and even the cost are the most problems associated with the usage of known antifungal agents.[45] Thus, the discovery of new antifungal agents will take the priority for enhancement treatment of various fungal infection, including dermatophytosis.

Conclusions

There is no part of the world can be cleared from infection with dermatophytosis. They involve about 40 different species. The contiguous nature of the dermatophyte infection makes it easy spread to infect healthy people, and also spreading from animal to human is high, it is worth to mention that spreading can be occurred in the same body of the infected person from location to another due to high contagious ability of these fungi. Dermatophytes can be classified according to the location in the environment or route of transmission into the following three groups: anthropophilic (transmitted from human to human), zoophilic (transmitted from animals to humans), and geophilic (transmitted from soil to human).

The skin, hair, and nail of all types of mammalian, including the human, are under the risk to develop dermatophytosis. The disease is mainly caused by different species of dermatophytes within the cutaneous layer of the skin. Dermatophytes revolutions appeared strongly as significant rising trend of this infection, especially in the last years. Tinea is the name of the disease caused by dermatophytes.

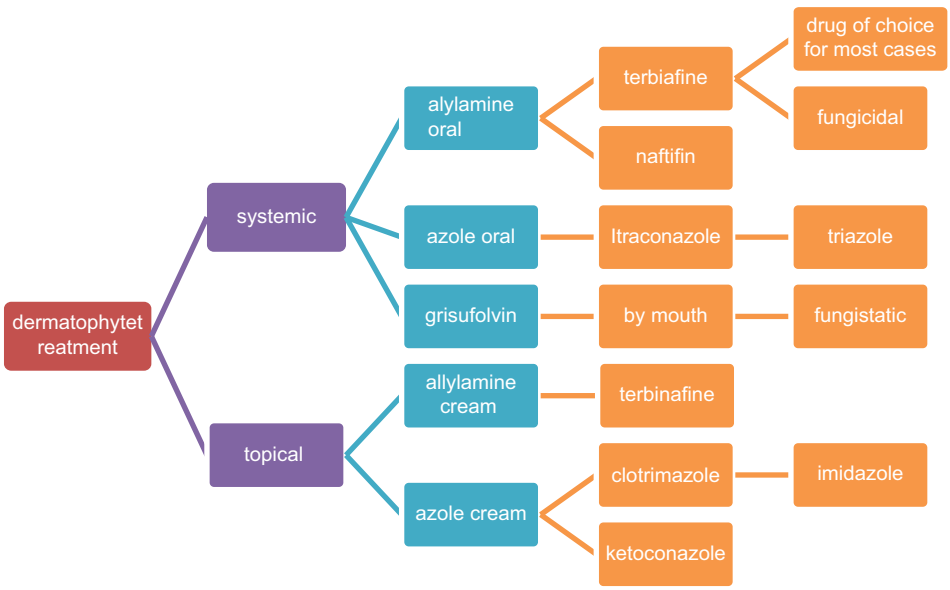

Figure 2: Most drugs used in dermatophytosis treatment

Dermatophytosis or tinea can be increased in the presence of several conditions such as overcrowding, dressing of occlusive clothes, increased urbanization, low socioeconomic status, contact with animals, and poor hygiene.

Enzymes produced by dermatophytes play a crucial role in pathogenesis. Due to less antifungal used to treat dermatophytosis, new drugs are demanded. The systemic antifungal drug used to treat dermatophytosis with some reverse effects, while the topical drug is safe and effective.

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Conflicts of interest

There are no conflicts of interest.

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