OPEN ACCESS

FUNGAL TERRITORY

2019, VOL. 2, NO. 2, 3-5

SCICELL

REVIEW ARTICLE

REVIEW OF FUNGAL SKIN INFECTIONS AND THEIR INVASION

Ayah Rebhi Hilles[1], Syed Mahmood[2,3*], Mohd Arifin Kaderi[1], Ridzwan Hashim[1]*

Address (es):
[1]Department of Biomedical Sciences, Kulliyyah of Allied Health Sciences, International Islamic University Malaysia, 25200 Kuantan, Pahang, Malaysia.
[2]Department of Pharmaceutical Engineering, Faculty of Engineering Technology, University Malaysia Pahang, 26300 Gambang, Pahang, Malaysia.
[3]Centre of Excellence for Advanced Research in Fluid Flow (CARIFF), University Malaysia Pahang, 26300 Gambang, Pahang, Malaysia.

*Corresponding author: ayah.hilles90@gmail.com and syedmahmood@ump.edu.my

ABSTRACT

Fungi have major roles in microbial community stability, human health, and disease (**Peleg** *et al.*, 2010). Genomic methodologies to identify fungal species and communities have been limited compared with those that are available for bacteria (**Dollive** *et al.*, 2012). Superficial mycoses infections are prevalent worldwide. They affect around 20% of the world's population, and this percentage continues to increase (**Ameen**, 2010).

Keywords: Skin infection, fungi, invasion, folicule

INTRODUCTION

Fungi have major roles in microbial community stability, human health, and disease (**Peleg** *et al.*, 2010). Genomic methodologies to identify fungal species and communities have been limited compared with those that are available for bacteria (**Dollive** *et al.*, 2012). Superficial mycoses infections are prevalent worldwide. They affect around 20% of the world's population, and this percentage continues to increase (**Ameen**, 2010).

SKIN INFECTIONS

The skin is the largest organ of the human body, which comprises about 15% of the total adult body weight. It has many important functions, such as preventing excess water loss from the body and protecting the body against external physical, biological and chemical assailants, (**Kanitakis**, 2002). Globally, the skin infection is ranked fourth among the top ten most common skin diseases (**Hay** *et al.*, 2014). The skin infection has a high prevalence rate which reaches up to 80 % in developing countries (**Ramamuthie** *et al.*, 2015). Lack of awareness and understanding of risk factors for skin infection is a major reason for the development of skin infections (**Goonmatee and Rajesh**, 2013). The skin works as a mechanical barrier which limits the invasion and growth of pathogenic fungi (**Harder** *et al.*, 1997). Skin protection established by keratinocytes and skin-resident T-cells is compromised in chronic skin disease and it has been suggested that the disturbance of the normal skin homeostasis causes an increased risk of infection (**Di Meglio** *et al.*, 2011). Intact skin protects from the external environment by maintaining a normal flora that is not conducive to the growth of pathogenic organisms. Primary skin and soft tissue infections (SSTIs) occur when pathogenic microorganisms invade the healthy skin, while secondary SSTIs occur when microorganisms infect the damaged skin. In both situations, the pathogenic microorganisms lead to damage the surrounding tissues, which cause an inflammatory response characterized by warmth, pain, and erythema (**Chahine** *et al.*, 2015).

FUNGAL SKIN INFECTION

Superficial fungal infections of the skin are among the most common diseases. it affects the outer layers of the skin, hair, and nails. The fungi may cause dermatological infections without involving tissue systemic invasion. The main groups of fungi leading to superficial fungal infections are dermatophytes, moulds, and yeasts. The dermatophytes that cause only superficial localised infections of the skin are grouped into three genera: *Microsporum*, *Epidermophyton*, and *Trichophyton.* Dermatophytes infect keratin and therefore cause diseases in body sites wherein keratin is present including the skin surface, hair, and nails. *Trichophyton rubrum* is the most prevalent cause worldwide for superficial dermatophytosis. Yeasts are not pathogenic, but an alteration in normal flora and colonisation then disease can occur. *Candida* normal inhabitant in the oropharynx, gastrointestinal tract, and vagina in some people, but in moist and wet conditions, *Candida* will overgrowth which can lead to superficial infections of the skin. *Candida albicans* can cause diseases in the skin, nails, viscera and mucous membranes (**Ho and Cheng**, 2010). Many human infections with environmental fungi reports describe infections caused by traditional and new agents with new mechanisms of infection. Fungal diseases remain a serious cause of illness and death. Much can be done to avoid the consequences of these infections, although environmental exposure to these agents may not be preventable in the society. Future research is needed to develop novel diagnostics, treatments, and vaccines against fungal infections (**Brandt and Park**, 2013).

Table 1 Gap analysis of the most common fungal skin infections

Fungal skin infection	Fungal species	Area infected	Symptoms	Treatment
Tinea pedis	*Trichophyton*, *Epidermophyton* or *Microsporum*.	It infects the foot.	It causes peeling, redness, itching, burning, and sometimes blisters and sores.	Terbinafine fluconazole or itraconazole
Tinea corporis	*Trichophyton*, *Microsporum*, or *Epidermophyton*	It can appear anywhere on the body	It is often accompanied by scaly skin. The outer part of the sore can be raised while the skin in the middle appears normal.	Itraconazole or terbinafine
Cutaneous candidiasis	*Candida albicans*	Yeast infections may affect nearly any skin surface on the body, but are most likely to occur in warm, moist, creased areas including the armpits and the groin.	It causes rash, patches that ooze clear fluid, pimple-like bumps and itching or burning Candida can cause diaper rash in infants and can cause infections of the nail. Oral thrush is a form of candida infection that is found in the mouth. Candida also causes vaginal yeast infections.	Clotrimazole, nystatin, fluconazole, voriconazole, amphotericin B, or echinocandins

Fungal infections are more prone to emerge after antibiotic treatment caused by the loss of the body's own bacterial flora (**Noterman and Nurmio**, 2016). Tinea capitis which was also known as herpes tonsurans, ringworm of the hair (**James** *et al.,* 2006) and tinea tonsurans. It is mainly caused by dermatophytes in the *Trichophyton* and *Microsporum* genera which invade the hair shaft. The clinical feature is typically single or multiple patches of hair loss. Ectothrix hair invasion is usually caused by *Microsporum gypseum, M. canis, M. distortum, M. ferrugineum, M. audouinii, M. nanum, and T. verrucosum*. Hyphae invade the hair shaft at the mid of the follicle, then it grows out of the follicle and covers the hair surface. The hyphae destroy the hair cuticle and cause tinea capitis infection including seborrheic dermatitis, "black dot" which refers to the breakage of hair follicles and inflammation. Inflammatory lesions of tinea capitis may develop abscesses, pustules or kerions which are edematous nodules with or without pustules (**Rapini** *et al.,* 2007).

FUNGI INVASION

Dermatophytes are aerobic fungi which invade the superficial keratinized layers of skin, hair, and nails. Three genera of fungi responsible for most dermatophytic infections i.e *Trichophyton, Microsporum,* and *Epidermophyton*.

FUNGI INVADE THE SKIN

Dermatophytes infect only the keratinized stratum corneum of the epithelial skin layers. Dermatophytes consider as the causative agents of dermatophytosis (tinea). They are parasitizing filamentous fungi that can infect the keratinized tissues which include the stratum corneum of the epidermis skin layers, nails and hairs. Dermatophytes induce a dermal inflammatory response which causes erythema and intense itching. The pathogenesis of tinea includes four steps, starting with the contact of infective spores with the skin then adherence to the superficial cells, after that the fungi invade to the keratin layers by secretion of keratinases which degrade the hard keratin into low molecular weight components and the last step is induction of inflammation (**Tyring** *et al.,* 2016).

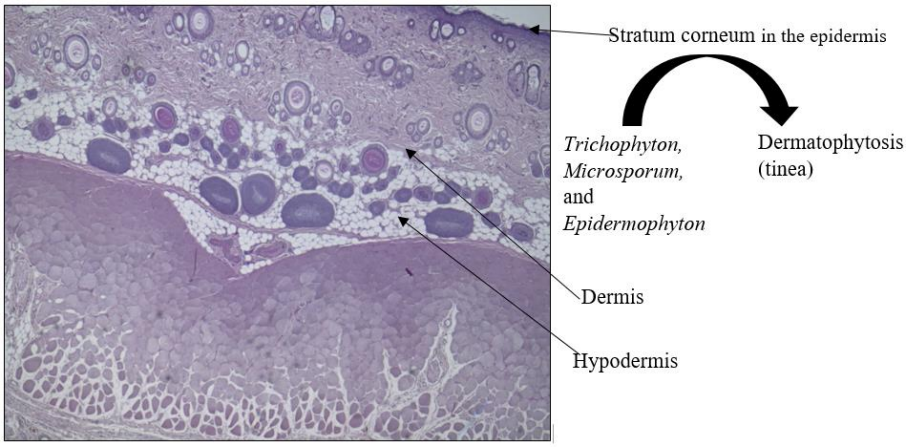

Figure 1 Histological features of rat skin tissue show a cross section of the skin layers (H&E, × 4). (Image captured by Ayah Rebhi Hilles).

FUNGI INVADE THE HAIR FOLLICLE

Tinea capitis is a superficial fungal infection of the scalp caused by *Trichophyton* and *Microsporum* genera that invade the hair shaft which formed of three layers (**medulla**, **cortex,** and **cuticle)**. The clinical features include patches of hair loss, sometimes accompanied by a 'black dot' pattern, inflammation, pustules, and itching. It is more common in pre-pubertal children, more often in boys than girls (**Baker** *et al.,* 2012).

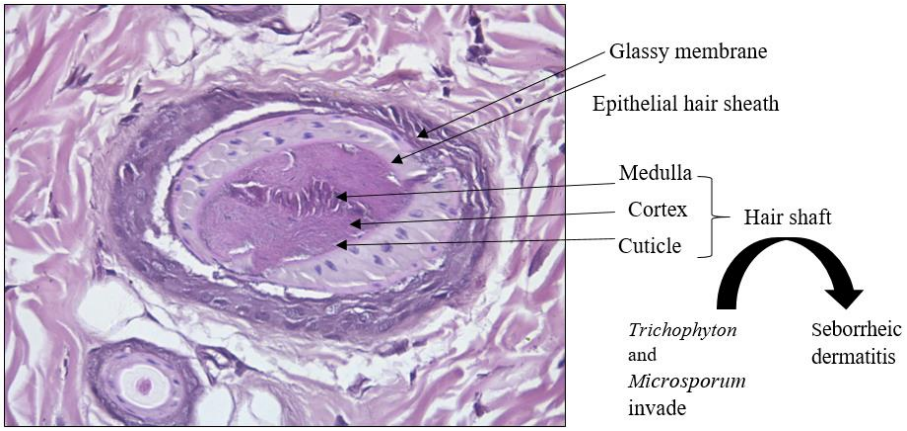

Figure 2 Histological features of the hair follicle in the rat skin tissue show a longitudinal section of the hair follicle (H&E, × 40). (Image captured by Ayah Rebhi Hilles).

FUNGI INVADE THE HAIR FOLLICLE BECAUSE OF THE SEBACEOUS GLAND

Malassezia is a genus of fungi which naturally found on the skin surfaces. The fungus is more common in areas with many sebaceous glands as it requires fat to grow but if the fungus grows rapidly, the natural renewal of cells will be disturbed, and dandruff will appear with itching (**Guého** *et al.,* 1996).

Seborrheic dermatitis is skin infection caused because of excess production of sebum from the sebaceous glands which attached to the hair follicles. The sebum contains high amounts of triglycerides and cholesterol and few of free fatty acids and. The rich sebum production triggers the proliferation of skin flora, yeast *Pityrosporon ovale* (also called *Malassezia furfur*). This excessive yeast proliferation leads to skin inflammation which causes temporary hair loss if the dermatitis is located on the scalp or other skin areas. Sometimes dermatitis causes scaly, oily and itchy inflamed skin.

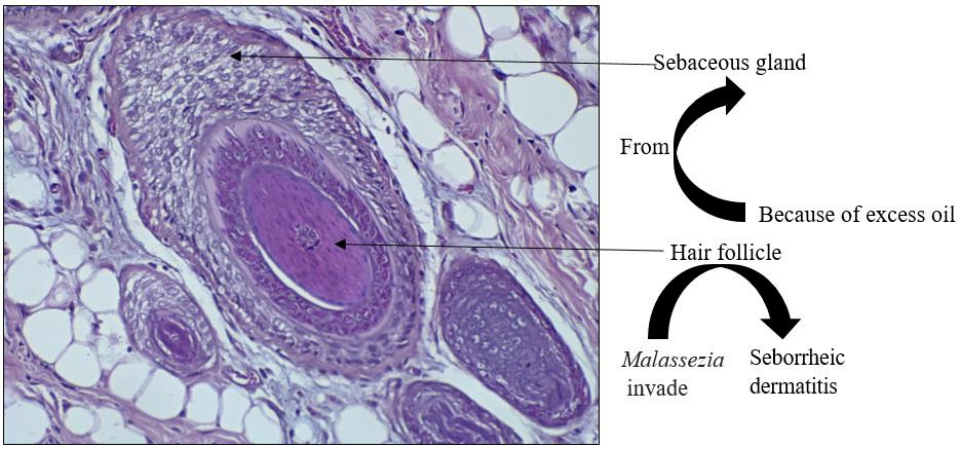

Figure 3 Histological features of the hair follicle and sebaceous gland in the rat skin tissue shows a longitudinal section of the hair follicle and sebaceous gland (H&E, × 40). (Image captured by Ayah Rebhi Hilles).

CONCLUSION

Superficial fungal infections occur in the outermost layers of the skin, nails, and hair. In recent years, the prevalence of these infections has risen steadily due to many factors, such as low socioeconomic status, poor skin health, low level of hygiene, personal hygiene, climatic conditions and level of awareness

Acknowledgment: This work was financially supported by a Research Grant (Project No. RDU 180371) from Universiti Malaysia Pahang (www.ump.edu.my), Malaysia, for which the authors are very grateful.

REFERENCES

Ameen, M. (2010). Epidemiology of superficial fungal infections. *Clinics in dermatology*, *28*(2), 197-201. https://doi.org/10.1016/j.clindermatol.2009.12.005.

Dollive, S. et al. A tool kit for quantifying eukaryotic rRNA gene sequences from human microbiome samples. *Genome Biol.* 13, R60 (2012). https://doi.org/10.1186/gb-2012-13-7-r60.

Peleg, A. Y., Hogan, D. A. & Mylonakis, E. Medically important bacterial–fungal interactions. *Nature Rev. Microbiol*. 8, 340–349 (2010). https://doi.org/10.1038/nrmicro2313.

Harder, J., Bartels, J., Christophers, E., & Schröder, J. M. (1997). A peptide antibiotic from human skin. *Nature*, 387(6636), 861. https://doi.org/10.1038/43088.

Di Meglio, P., Perera, G. K., & Nestle, F. O. (2011). The multitasking organ: recent insights into skin immune function. *Immunity*, 35(6), 857-869. https://doi.org/10.1016/j.immuni.2011.12.003.

Chahine, E. B., Sucher, A. J., & Knutsen, S. D. (2015). Tedizolid: a new oxazolidinone antibiotic for skin and soft tissue infections. *The Consultant Pharmacist®,* 30(7), 386-394. https://doi.org/10.4140/TCP.n.2015.386.

Kanitakis, J. (2002). Anatomy, histology and immunohistochemistry of normal human skin. *European Journal of Dermatology*, *12*(4), 390–401.

Hay, R. J., Johns, N. E., Williams, H. C., Bolliger, I. W., Dellavalle, R. P., Margolis, D. J., ... & Michaud, C. (2014). The global burden of skin disease in 2010: an analysis of the prevalence and impact of skin conditions. *Journal of Investigative Dermatology*, 134(6), 1527-1534. https://doi.org/10.1038/jid.2013.446.

Ramamuthie, G., Verma, R. K., Appalasamy, J., & Barua, A. (2015). Awareness of risk factors for skin infections and its impact on quality of life among adults in a malaysian city: a cross-sectional study. *Tropical Journal of Pharmaceutical Research*, 14(10), 1913-1917. http://dx.doi.org/10.4314/tjpr.v14i10.25.

Goonmatee, K., & Rajesh, J. (2013). What factors contribute to a higher frequency of skin infections among adults in Mauritius?. *Our Dermatology Online*, 4(3), 297. https://doi.org/ 10.7241/ourd.20133.72.

Ho, K. M., & Cheng, T. S. (2010). Common superficial fungal infections-a short review. *Medical bulletin*, 15(11), 23-7.

Brandt, M. E., & Park, B. J. (2013). Think fungus—prevention and control of fungal infections. *Emerging Infectious Diseases*, 19(10), 1688. http://dx.doi.org/10.3201/eid1910.131092.

Noterman, H., & Nurmio, A. (2016). Infectious diseases in children and treatment at home: *guidebook for parents.*

Rapini, R. P., Bolognia, J. L., & Jorizzo, J. L. (2007). Dermatology: 2-Volume Set. St. Louis: Mosby.

Tyring, S. K., Lupi, O., & Hengge, U. R. (2016). *Tropical Dermatology E-Book*. Elsevier Health Sciences.

Guého, E., Midgley, G., & Guillot, J. (1996). The genus Malassezia with description of four new species. *Antonie van leeuwenhoek*, *69*(4), 337-355. https://doi.org/10.1007/BF00399623.

Baker, R. D., Angulo, O. A., Barroso-Tobila, C., Carbonell, L. M., Cespedes, R., Chick, E. W., ... & Graham, J. H. (2012). *The pathologic anatomy of mycoses: human infection with fungi, actinomycetes and algae* (Vol. 3). Springer Science & Business Media.