Introduction

Onychomycosis is chronic fungal infection of finger and toe nails. It accounts to for up 50% of all nail problems including dermatoses affecting the nail like: Psoriasis, Lichen Planus, Alopecia Areata and Eczema and also the developmental abnormalities of nails like: Anonychia, Nail Patella syndrome and Pachyonychia Congenita **(Sigurgeirsson and Steingrimsson, 2004).** It has been estimated that 15% to 20% of individuals between 40-60 years of age may suffer this problem **(Jesudanam et al., 2002).**

Toenails are affected more often than fingernails and the incidence is greater in older adults **(Evans,2000).** Individuals who are especially susceptible include those with chronic diseases such as diabetes, circulatory problems, smokers, patients with psoriasis and those with diseases that suppress the immune system (e.g. HIV-positive patients, extremes of age, patients on long term corticosteroids therapy). Other risk factors include a family history, previous trauma to the nails, warm climate, and occlusive or tight footwear **(Gupta et al., 2004).**

The clinical presentation of onychomycosis often involves hyperkeratosis with thickening and discoloration of the nail plate, althoughearlyinfection of the nail plate may not be clinically appreciated. A previous histological study identified dermatophytes in 48.2% of 311 dystrophic nails **(Walling and Sniezek, 2007).**

The causative agents of onychomycosis include dermatophytes, to a lesser extent non dermatophyte moulds and rarely, yeasts of the Candida species **(Evans,2000).**

In jobs that need a healthy decreased quality of life and social isolation; also it may lead to Onychomycosis can lead to functional impairment, occupational hinder especially appearance of nails as: cooks, sales representatives and fashion models **(Elewski, 1998).**

Onychomycosis is classified clinically as distal and lateral subungual onychomycosis (DLSO), superficial white onychomycosis (SWO), proximal subungual onychomycosis (PSO), candidal onychomycosis and total dystrophic onycho-mycosis **(Summerbell,2007).**

Nail diseases are often very troublesome to thepatient **(Drake et al., 1999; Lubeck, 1998)** and can be diagnostically challenging even to the experienced dermatologist **(Korting and Schaller, 2001; Seebacher et al., 2007)**. Especially, onychomycosisis a common problem **(Burzykowski et al., 2003; Kaur et al., 2008)** and can sometimes be difficult to be distinguished from other nai ldisorders like psoriasis, lichen ruber or eczematous nails **(Allevato, 2010; Oppel and Korting, 2003).** The development of optimised antimycotic.

Onychomycosis is very difficult and sometimes impossible to treat, and therapy is often long-term with high relapse rates 50 – 85 %. Several management and treatment regimens were designed

to control and cure this disease such as palliative care, topical as well as systemic drugs **(Gupta, 2003)**. Among the orally delivered systemic drugs terbinafine, itraconazole and fluconazole are most frequently used, but with several unpleasant side effects as headache, gastrointestinal symptoms, liver enzyme abnormalities **(Scher, 1999).**

Nail debridement chemically or surgically is another treatment option, but it is considered by many to be primitive compared with topical or systemic treatment (**Donald et al., 2002**). The choice of therapy is influenced by the presentation and severity of the disease, other medications that the patient is taking, physician and patient preference, and cost **(Gupta et al., 2003).**

Recently, a novel non-invasive approach for treatment of onychomycosis is the application of laser energy to the nail plate targeting the fungal cells themselves. By using a laser with a specific wavelength of laser light energy, the fungus could be directly targeted in the nail and heated to the point it is killed, but without burning the surrounding tissue and with leaving the skin and nail intact **(Kozarev and Vizintin, 2010).**

Aim of the Essay

The aim of this essay is to review and discuss updated aspects of the diagnosis, etiology and therapy of onychomycosis.

Onychomycosis

Definition:

Onychomycosis is a common persistent fungal infection of the fingernail or /& toenail **(Jesudanam et al., 2002).** It is a general term used for any fungal infection of the nail that can be caused by dermatophytes, yeasts or other non-dermatophyes moulds (NDMs) **(Jennings et al., 2002).** This contrasts with the term tinea unguium that is specifically used for infection of the nails caused strictly by dermatophytes **(Zaias, 1990).** It may involve any component of the nail unit, including the nail matrix, nail bed, or nail plate **(Zaias, 1990).**

Nail Apparatus

Nails are keratinous horny plates that form protective coverings on the dorsal surface superior to the distal or ungual phalanges of the fingers and toes **(Daniel, 2004)**.

It is important to know the structural and functional organization of the nail unit and the process of nail growth to understand pathogenesis of fungal infection of the nail unit **(Haneke, 2006).**

A. Structure of the Nail unit:

The term "nail unit" is used to describe the nail and its surrounding structural components.

Anatomic structures of the nail (Figures 1 & 3) include, from proximal to distal; the nail matrix (nail root) and the

lunula, the proximal nail fold, eponychium, the cuticle the lateral nail folds (perionychium), the nail plate, the nail bed, the onychodermal band and the hyponychium **(Rich, 2005 and Ximena and Gregor, 2006).**

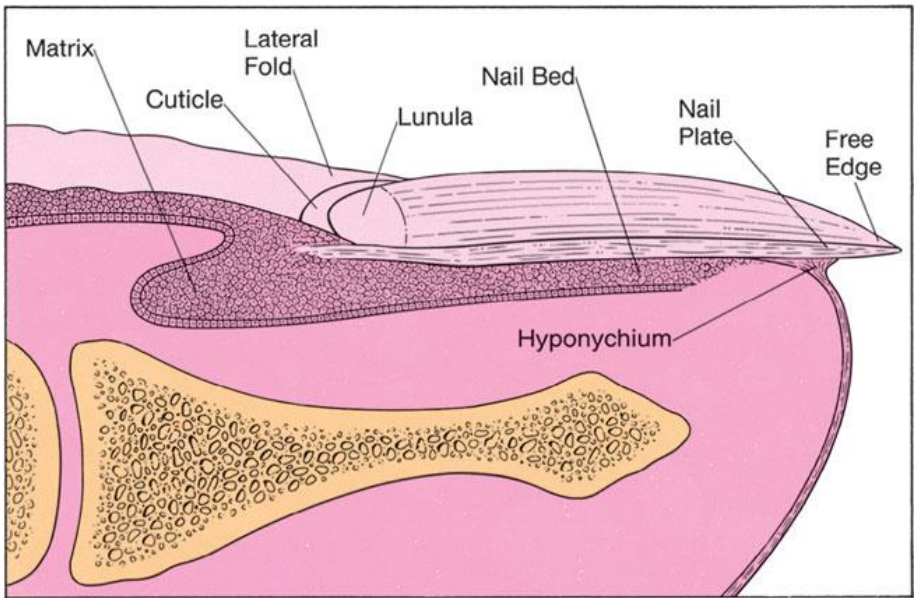

Figure (1): Schematic drawing of nail anatomy sagittal section ***(Wolff, 2009).***

1. **The matrix (Nail root)**: it is the germinative epithelium that gives rise to majority of nail plate. It consists of proximal (dorsal) and distal (intermediate) portions. The proximal portion of the matrix lies beneath the nail folds and the distal curved edge. It can usually be seen through the nail plate as the lunula (half moon) which is whitish, crescent-shaped and contains nerves, lymph, blood vessels **(Elewski, 1998).** The proximal matrix forms the superficial (dorsal) part of the nail plate and the distal matrix makes the under-surface (ventral) part of the nail plate (Figure 2) (**De-Berker et al., 2007).** Its proliferation activity is higher in its proximal portion than

distally so that more nail substance is formed proximally and the nail plate achieves a natural convex curvature from proximal to distal **(Rich, 2005).** It has lateral matrix horns that reach further proximally than the central part of the matrix **(Haneke, 2006).**

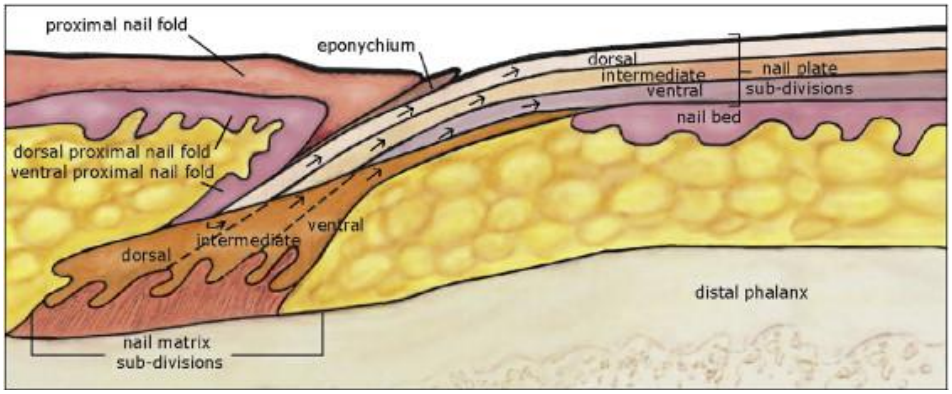

Figure (2): The proximal matrix forms the superficial part of the nail plate and the distal matrix makes the under-surface part of the nail plate **(Jiaravuthisan et al., 2007).**

2. The nail folds:

- The proximal nail fold is the cutaneous fold covering the proximal end of the nail **(Haneke, 2006).** It is continuous with the cuticle, which is the horny end product that is shed from the underside of the proximal nail fold **(Elewski, 1998 and Rich, 2005).**

- The lateral nail folds (the paronychium) are the cutaneous folds on the lateral sides of the nail, where it meets the skin of the finger **(Zook, 2003).** Its function is to surround, support and protect the nail **(Rich, 2005).**

3. The Eponychium:

It is the small band of epithelium that binds the nail to the underlying skin. It is located proximally on the dorsal surface of the nail extending from the base of the nail. Precisely, it is located at the end of the proximal nail fold above the cuticle **(Elewski, 1998).**

4. The nail bed:

It is the vascular bed beneath the nail plate extending from the lunula to the hyponychium. It is composed of two layers, the deeper dermis, which is the living tissue fixed to the bone containing capillaries and glands; and the superficial epidermis, which is the layer just beneath the nail plate that moves forward with it. The epidermis is attached to the dermis by tiny longitudinal "grooves" known as the matrix crests **(De-Berker et al., 2007)**, forcing the nail plate to grow forwards **(Perrin, 2008).** The nail bed is sometimes called the sterile matrix and probably contributes some cells to the under-surface of the nail plate, allowing the nail to grow continuously while adhering to the nail bed **(Rich, 2005).**

5. The nail plate: it is the smooth translucent structure that is the end product of the keratinocyte differentiation in the nail matrix **(De-Berker et al., 2007).** It is formed of a strong flexible material made of several layers of dead, flattened mechanically and chemically resistant sheet of compacted keratinized cells. Nail hardness is mainly due to the disulfide bonds found in the keratin in the nail plate. It also contains

0.1% calcium, which contributes a little to the hardness of the nail plate **(Rich, 2005).**

6. **The Hyponychium:** is the epithelium located beneath the nail plate at the junction between the free edge and the skin of the fingertip **(Elewski, 1998).** It forms a seal that protects the nail bed and obliterates the distal groove called onychodermal band located just under the free edge, in that portion of the nail where the nail bed ends **(Perrin, 2008).**

7. **The onychodermal band:** it is an ill-defined transverse band of a deeper pink, approximately 1 to 1.5 mm in width that marks the transition of the nail bed to the hyponychium. Its integrity is important for the health of the nail bed **(Haneke, 2006)**, as it represents the first barrier to penetration of materials beneath the nail plate **(De-Berker et al., 2007).**

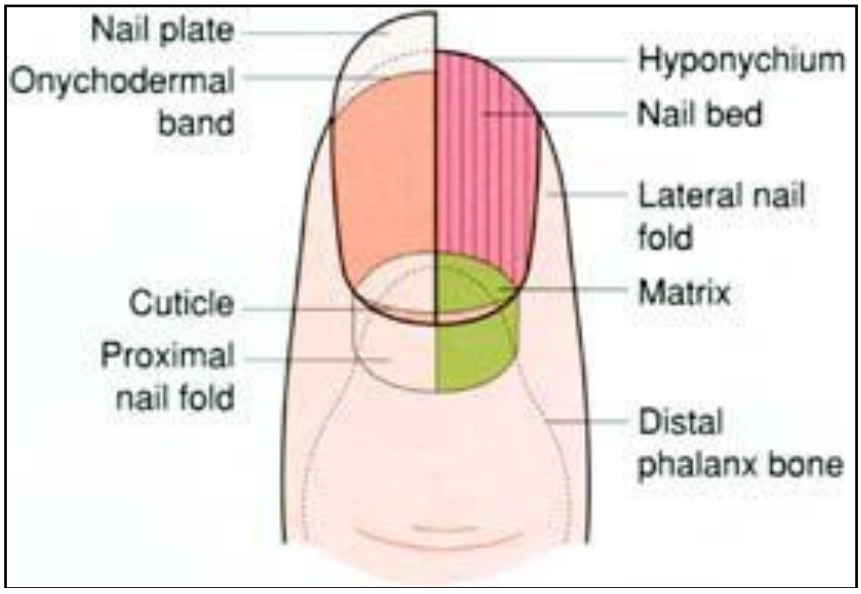

Figure (3): A diagram showing front view of nail anatomy **(Rich, 2005).**

B. Types of cells in the nail apparatus:

1. Nail matrix:

The nail matrix is made of epidermis and dermis. It is composed of squamous epithelium but has no granular layer. It has long rete ridges characteristically descending at a slightly oblique angle, their tips pointing distally. Laterally, the matrix rete ridges are less marked, whereas those of the nail bed and nail folds become prominent. Distally, there is often a step reduction in the epithelial thickness at the transition of the matrix with the nail bed which represents the edge of the lunula. Germinal cells in the matrix become larger and paler and eventually the nucleus disintegrates. There is progression with flattening, elongation and further pallor. There are some melanocytes and dendritic cells found in the epibasal layers and most prominent in the distal matrix. There is only a thin layer of dermis dividing the matrix from the terminal phalanx. This has a rich vascular supply and an elastin and collagen infrastructure giving attachment to periosteum **(De-Berker et al., 2007).**

2. Nail folds:

The lateral and proximal nail folds are similar in structure to the adjacent skin but are normally devoid of demographic marking and sebaceous glands. Keratinization within the nail folds proceeds via keratohyaline formation in the granular layer **(De-Berker et al., 2007).** The dorsal part of the proximal nail fold is formed of epidermis and dermis that is the continuation of the skin of the dorsal digit with sweat gland but no hair follicles and sebaceous glands. The skin of the ventral surface of proximal nail fold is thin, does not show rete ridges- dermal papillae pattern or epidermal appendage **(Rich, 2005).**

It is made of deep epidermal layers -as it has no granular layer- and dermis. There is no subcutaneous tissue in the nail bed, so immediately beneath the nail bed lies the periostium of the distal phalanx **(Rich, 2005).**

The epidermis of the nail bed is thin but becomes thicker at the nail folds where it develops rete ridges. The dermis is sparse, with firm collagenous adherence to the underlying periosteum and no sebaceous or follicular appendages. Sweat ducts can be seen at the distal margin **(De-Berker et al., 2007).**

3. Nail plate:

It is composed of multilayered, stacked sheet of compacted keratinized epithelial cells that are intimately fused and translucent. These cells derived from anucleate onychocytes that arise from the germinal matrix epithelium where the proximal matrix gives rise to the superficial (dorsal) part of the nail plate and the distal matrix makes the under-surface (ventral) part of the nail plate (**De-Berker et al., 2007).** The cells of the proximal part of the nail plate are not completely anucleated (parakeratotic cells in horny layer) so they are whitish in colour **(Ximena and Gregor, 2006).**The nail plate appears pink because it transmits the coloration of blood vessels of the nail bed beneath **(Daniel, 2004).**

4. The hyponychium:

It has a granular layer unlike the matrix and nail bed **(Rich, 2005).** Cells of the hyponychium are larger than cells of the nail plate proper **(Daniel, 2004).**

C-Function:

The human nail can be considered to have many mechanical and social functions, the most prominent of which are:

- Fine manipulation.
- Scratching.
- Physical protection of the extremity.
- A vehicle for cosmetics and aesthetic manipulation.
- The nail provides counterpressure to the pulp that is essential to the tactile sensation involving the fingers

(De-Berker et al., 2007)

The nail organ is an integral part of the digital tip, it is both our most versatile tool and one of the most important sensory organs **(Haneke, 2006)**. The function of the human nail is to assist in picking up small objects, to protect the distal digit, to improve fine-touch sensation and to enhance the aesthetic appearance of the hands. The flat nail on the end of the human finger allows for increased sensory perception in the pad of the finger by compressing sensory end organs between the volar skin and the nail, which in turn provides for efficient and accurate apprehension of small objects. It also serves to protect the very sensate fingertip, as well as functioning as a temperature regulator. A complete understanding of the anatomy and physiology of the nail is essential to identify its mysteries and its response to pathological processes **(Rich, 2005).** Nail loss or deformity can be not only aesthetically compromising, but also a functional problem **(Zook, 2003).**

D-Nail growth:

Nail growth occurs by the addition of keratinizing cells from the nail matrix onto the nail plate over the nail bed **(Mccarthy, 2004).**

Fingernails, unlike hair, grow continuously, at a rate of approximately 0.1 mm/day or 3 mm a month. Toenails grow at about one-half to one-third the rate of fingernails. The mean toe nail growth rate is 1mm/month, this rate of growth is often decreased in the presence of peripheral vascular disease, onychomycosis and in the elderly. A fingernail regenerates in 4–6 months, toenails in 8–12 months or more. Certain states affect the rate of nail growth; for example, nails grow faster during pregnancy and in psoriasis **(Rich, 2005).**

Population studies on nail growth have given the general findings that there is little marked seasonal change and nails are unaffected by mild intercurrent illnesses. The height or weight of the individual made no significant difference. Sex makes a small difference in early adulthood, with men having significantly faster linear nail growth up to the age of 19. They continue to do so with gradually diminishing significance levels, up to the age of 69, when there is a cross-over and women's nails grow faster than males'. However, males continue to have a greater rate of nail growth throughout life if volume was measured, and not length. Children under 14 have faster growth than adults. Pregnancy may increase the rate of nail growth and poor nutrition may retard it. Temperature is an influence with unclear effects **(De-Breker et al., 2007).**

Epidemiology of Onychomycosis

It is the most common disease of the nails and constitutes about half of all nail abnormalities **(Szepietowski and Salomon, 2007)**. It affects as much as 8% of the general population and it seems to increase with age **(Elewski, 1998)**. Toenail onychomycosis is about 4 to7 times more frequent than finger nail disease **(Ellabib et al., 2002)**. It accounts for one third of all fungal skin infections **(Migdley et al., 1994)** and up to 50% of all nail diseases worldwide (including psoriasis, atopic dermatitis, nail trauma, contact irritants, and lichen planus) **(Drake et al., 1996).**

It affects males more commonly than females. However, candidal infections are more common in women than in men **(Elewski, 1998; Smith et al., 2001).**

It has been estimated that 15% to 20% of individuals between the ages of 40-60 years may suffer from this problem **(Jesudanam et al., 2002).**

Children have infection rates 30 times lower than adults. The reason for this decrease may be due to, reduced exposure to fungus because of less time spent in environments containing pathogens, faster nail growth, smaller nail surface for invasion and lower prevalence of tinea pedis. Onychomycosis prevalence in children younger than 18 years ranges from 0% in USA up to 2.6% in Guatamala **(Gupta et al., 1997c).**

Contact with the source of the infection constitutes a risk factor; for example, *Trichophyton verrucosum* commonly infects the faces of farmers who lean against their cows as they milk them **(Winn, 1996).**

Dermatophytes are the fungi most commonly responsible for onychomycosis in the temperate western countries **(Chi et al., 2005).** Non dermatophtes moulds **(**NDMs) are more frequent in tropical and subtropical areas with a hot and humid climate **(Haneke, 1991 and Chi et al., 2005).**

Incidence and prevalence:

According to small studies, prevalence of onychomycosis varies from 4% to 18% depending upon the age, geographic distribution and population studied **(Erbagci, 2005).**

However, the incidence of onychomycosis has been reported to be 2% to 13% in North America **(Raujo et al., 2003)**, while a multicenter survey in Canada showed the prevalence of onychomycosis at 6.5% **(Summerbell, 1997).**

In addition, studies in the United Kingdom, Spain, and Finland found prevalence rates of onychomycosis to be 3% to 8% **(Iorizzo et al., 2007).**

The 'Achilles' project which is the largest survey of onychomycosis in 20 European countries, revealed an incidence rate of 29% **(Burzykowski et al., 2003).**

Unlike the Western countries where it is a frequent cause of nail disorder, the prevalence of onychomycosis in South East