

Malassezia infections: Diagnostic perspective and treatment approach in Africa

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Abstract: Background: *Malassezia* is a normal flora of human skin. Overtime, research has shown that these yeasts cause diseases such as *Malassezia* folliculitis, pityriasis versicolor, seborrheic dermatitis and psoriasis. The study was aimed at reviewing the status of *Malassezia* skin diseases in Africa and the modalities for their treatment. **Methods:** With a narrative approach, the review made use of documented findings from previous works, and multiple data base were consulted for the literature including PubMed, MEDLINE, Google scholar, systematic reviews, observational studies, Cochrane databases, randomized controlled trials. These were assessed through Google search. **Results/Discussion:** This review showed that the highest prevalence of pityriasis versicolor occurred in Central African Republic (17.9%) while Mali (1.6%) had the least prevalence. The disease was more common on the face of adolescence and young adults. Nigeria recorded the highest prevalence for Seborrheic dermatitis (12.6%). Atopic dermatitis had its highest and lowest prevalence in Cote d'Ivoire (9.2%) and Tunisia (0.65%) respectively. Psoriasis was reported more in East Africa (2.6-3.3%) compared to West Africa (0.05-0.3%). Treatment of these diseases involves the use of topical and systemic antifungal agents and/or the combination of both for more effectiveness. **Conclusion:** There is need for improvement in diagnostic techniques used for these diseases and more research is required in order to ascertain the actual prevalence of these diseases in Africa.

Key words: *Malassezia* infections, presentations, diagnosis, treatment, Africa

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I. Introduction

Malassezia species belong to the Basidiomycete class of fungi. They cause skin diseases and are lipophilic (Sugita *et al.*, 2010). The genus *Malassezia* is composed of about 14 species which colonize human or animal skin. These include: *Malassezia furfur*, *Malassezia pachydermatis*, *Malassezia sympodialis*, *Malassezia globosa*, *Malassezia restricta*, *Malassezia slooffiae*, *Malassezia dermatitis*, *Malassezia japonica*, *Malassezia nana*, *Malassezia yamatoensis*, *Malassezia caprae*, *Malassezia obtuse* etc (Castellá *et al.*, 2013).

Malassezia globosa and *Malassezia restricta* are the most frequently found on human skin in health and disease but *Malassezia sympodialis* and *Malassezia furfur* are usually found in human diseased skin (Gaitanis *et al.*, 2013). Skin diseases caused by *Malassezia* species has a worldwide distribution affecting many individuals across the globe. *Malassezia* is a normal skin flora, but also an opportunistic pathogen.

The pathogenesis of *Malassezia* species and skin diseases has been controversial. They have been implicated in skin diseases with heavy fungal load but without inflammation. However, inflammation occurs in skin disorders such as seborrheic dermatitis, psoriasis, atopic dermatitis and folliculitis, where their pathogenesis role is unclear (Crespo *et al.*, 2010). The interaction between *Malassezia* yeasts and the skin is complex. It involves enzyme produced by the fungi, the fungal cell wall, metabolic products and the epidermis cellular components (Saunders *et al.*, 2012).

Malassezia infections are among the neglected superficial fungal infections worldwide, especially in the tropics. This review was aimed at the types, distribution and diagnosis of *Malassezia* infections in Africa and the treatment modalities of the disease.

Types and presentation of *Malassezia* infections

a. Pityriasis versicolor

The disease is an innocuous, chronic, superficial infection, localized on the stratum corneum of the skin. It presents as itchy oval to round lesions with defined edges on the trunk, the upper and lower arm and sometimes scaly (Gosh *et al.*, 2008). It is also known as tinea versicolor, dermatomycosis furfuracea or tinea flava (Rapini *et al.*, 2007).

Adolescents and young adults are more prone to Pityriasis versicolor especially those with high sebaceous gland activity. The most common *Malassezia* species isolated from lesions are *Malassezia sympodialis* and *globosa*. Others include *Malassezia slooffiae* and *Malassezia furfur*. However, *Malassezia furfur* is the most common isolate in warm climates (Guého-Kellermann *et al.*, 2011; Theodore *et al.*, 2014).

Most persons with pityriasis versicolor are healthy as the causative yeasts *Malassezia furfur* is a normal skin flora. The pigmentary changes characterized by this infection follow the inhibition of melanin formation by azelaic acid produced by the yeasts in the epidermis. It may take several months for the colour change to become visible and the skin discoloration is not permanent (Nura *et al.*, 2016).

b. Seborrheic Dermatitis

This is a chronic inflammatory dermatomycoses which appear as red macules or plaques with scaling and itching. The lesions occur on seborrheic areas which include: the face, axilla, chest, scalp, back and groin (Luis *et al.*, 2018). The reported prevalence of seborrheic dermatitis in the overall adult population ranges from 1 to 5% and the disorder can affect any ethnicity (Fritsch and Reider, 2003).

Seborrheic dermatitis is commonly caused by *Malassezia furfur*, *Malassezia globosa*, *Malassezia restricta*, although *Malassezia sympodialis*, *Malassezia obtuse*, *Malassezia slooffiae*, and *Malassezia yamatoensis* have been implicated (Sugita *et al.*, 2010).

Lesions have poorly defined borders, they appear red, pink-yellow, or brown and are scaly. They are often hypo pigmented on the African skin. The predilection of the yeasts depends on the state of health of the patient. In healthy people the face and scalp are mostly affected while in the HIV-infected, the armpits and groins become super infected. Seborrheic dermatitis can give rise to social problems, especially with severe to moderate scaling of the scalp (Luis *et al.*, 2018). Factors that may predispose to infection includes: stress, immunologic factors and climate (Naldi, 2009).

c. Atopic dermatitis

This is a cutaneous disorder which is chronic and begins in infancy, childhood or adolescence (Umuro *et al.*, 2010). Atopic dermatitis has been proven to be associated with *Malassezia globosa*, *Malassezia furfur*, *Malassezia sympodialis* and *Malassezia restricta* (Saunders *et al.*, 2012). The disease occurs commonly in individuals with allergic rhino-conjunctivitis and asthma, or in family circles (Spergel, 2006). Infantile atopic dermatitis occurs in children ≤ 2 years.

Characteristic lesions appear on the forehead, cheeks, face and scalp with oozing itchy eczema-like rash. It can also affect the hands, feet and trunk. Intense itching may lead to poor concentration at school resulting in poor academic performance. In the adolescents, the face, neck and flexures are affected (Umuro *et al.*, 2010).

In Nigeria, the disease is on the increase among infants in families with history of asthma, allergic rhinitis and conjunctivitis (Nnoruka, 2004).

d. Malassezia folliculitis

Malassezia folliculitis also known as *Pityrosporum* folliculitis occurs when there is blockage of the hair follicle by *Malassezia* yeasts. The production and breakdown of free fatty acids in the sebaceous glands lead to inflammation of the skin and hair follicle (Triana *et al.*, 2017). *Pityrosporum* folliculitis is a condition in which the hair follicles of the sebaceous areas (upper trunk, shoulders, and occasionally head and neck) are infected with *Pityrosporum* (*Malassezia*) yeasts, resulting clinically in inflammatory papules and pustules (Levin, 2018). This disease was initially implicated in immuno-compromised patients, but cases have been reported in immunocompetent patients (Bahlou *et al.*, 2018).

Malassezia species are present on an estimated 92% of normal skin flora globally. Their prevalence is highest in areas of high heat and humidity (Levin, 2018). *Pityrosporum* folliculitis typically affects teenagers and young adults, presumably due to their relatively active sebaceous glands. Since *Pityrosporum* yeasts cannot grow without exogenous lipids, they use the triglycerides found in human sebum as fuel. Individuals who are immunocompromised, diabetic, or taking oral antibiotics or systemic corticosteroids are at increased risk (Levin 2018).

e. Psoriasis

Psoriasis is a disorder of the skin characterized by periods of lessening of symptoms and reactivity. It is chronic and papulosquamous in nature and caused by *Malassezia furfur*, *Malassezia restricta*, and *Malassezia globosa* (Gaitans *et al.*, 2016). It is not common on dark skins and in the tropics. Occurrence in African-Americans is similar to that of West Africans suggesting genetic ancestry (Ayanlowo and Akinkugbe, 2016).

Epidemiology of *Malassezia* infections

i. Pityriasis versicolor

Pityriasis versicolor has a worldwide distribution, but common in the tropics (Kaur *et al.*, 2013). The predisposing factors are humid environment, excessive sweating, occlusion, high plasma cortisol levels, immunosuppression, malnutrition and genetically determined susceptibility (Nura *et al.*, 2016).

In Nigeria, Akpata *et al* (1990) in Cross River State, reported (3.7%) mycologically proven lesions of pityriasis versicolor among school children. They reported a higher prevalence of (6.3%) in children aged 12-16 and the presence of more lesions on the face than other parts of the body. In another study carried out in the South western part of Nigeria by Olaide *et al* (2014) in Ile-ife, the prevalence was higher 4.4%. It was also reported as one of the most common superficial fungal infection among school children. The 4.4% prevalence was similar to the 4.6% and 4.7% reported in Ibadan, South-Western Nigeria, and in Abakaliki, South-Eastern Nigeria by Ogunbiyi *et al* (2005) and Uneke *et al* (2006) respectively.

The prevalence in other African countries was: 16.6% in Central African Republic (Bélec *et al.*, 1991), 1.6% in Bamako, Mali, (Olaide *et al.*, 2014) and 8.0% in Northern Malawi (Pönnighaus *et al.*, 1996). Rates of infection were generally higher among males than females.

ii. Seborrheic dermatitis

In a study carried out in Ebonyi State University Teaching Hospital, Abakaliki, Nigeria, Okoh *et al* (2018) recorded 12.6% prevalence for seborrheic dermatitis. It was also reported as the third most common eczematous disorder. The prevalence of seborrheic dermatitis is low in children aged $\leq 1-12$ years in Ghana, Gabon and Rwanda (Hogewoning, 2013; Komba and Mgonda, 2010). However, it is frequently seen in HIV patients of all age groups. Biobelemoye and colleagues (2016) isolated *M. pachydermatis* in their study. This species is known to be found in pet animals which suggest a zoonotic transmission

iii. Atopic dermatitis

In a study conducted in Côte d'Ivoire by Ahogo *et al* (2017), the prevalence of atopic dermatitis in children was 9.2%. Lesions were dry, oozing, and lichenified. These lesions were found in the skin folds, trunk, legs and the face. The disease was common in children aged 2 to 5 years. More than half of the patients had a history of atopy. These were mainly dry lesions most often triggered by dust

Elsewhere in Tunisia, atopic dermatitis was diagnosed in ten of the 1522 examined children, with a prevalence of 0.65%. The principal site was the Knees, followed by the elbows. The ankles and around the eyes were also affected. No localization around the neck was found. First-degree family member with atopic dermatitis seemed to be the predisposing factor (Amouri *et al.*, 2011).

iv. Psoriasis

The prevalence of psoriasis in Africa is low. Ayanlowo and Akinkugbe (2016) reported 1.13% (124/11,015) in their study in Nigeria. Psoriasis affects about 1-3% people globally, but is rare in the Africans and North American Indians (Ayanlowo and Akinkugbe, 2016). The study by Nnoruka, (2005) reported a frequency of 0.6-1.5% among individuals attending dermatology outpatients in different parts of Nigeria. A recent study by Ayanlowo and Akinkugbe (2016) on the survey of dermatology patients in Nigeria revealed a reduction in the rate of the infection 0.1-0.5%.

Chandran (2013) reported a lower prevalence (1.3%) in African-Americans compared to that in Caucasians 2.5%. The prevalence of psoriasis was reported to be higher in East Africa than West Africa (Ayanlowo and Akinkugbe, 2016). The prevalence in West Africa is similar to that found among the African-Americans. This was thought to be due to the similarity in genetic ancestry (Ayanlowo, 2016). It is however, more common in women (Meffert *et al.*, 2015).

Africans have been postulated to either lack the psoriasis susceptibility gene or have genetic factors that promote resistance to psoriasis (Ayanlowo and Akinkugbe, 2016). Dietary factors have also been thought to partly contribute to the low prevalence of psoriasis in Africans (Namazi, 2004). The African staple diet particularly corn, is rich in linolenic acid, a precursor of prostaglandin E2 (PGE2); and low in poly-unsaturated fatty acids; encouraging overproduction of PGE2; suppressing cellular immunity underlying psoriasis; and directly block T-cell signaling and interleukin-2 (IL-2); ultimately reducing T-cell proliferation (Namazi, 2004).

v. *Malassezia* folliculitis

Much work has not been done on *Malassezia* folliculitis in Africa, but in Tunisia, the report by Levin (2018), revealed cases on the back, arm and chest of the subjects.

Diagnosis of *Malassezia* infections

Pityriasis versicolor

The diagnosis of pityriasis versicolor is based on the morphology of the lesion. Microscopy of KOH mounts of skin scraping from lesions is helpful (Nura *et al.*, 2016). Typical characteristic "spaghetti and meatballs" appearance of the yeasts and short hyphae is revealed upon microscopic examination. Culture is required if doubt arises.

Seborrheic dermatitis

This is based on history and clinical examination. Patient's age, sites of lesion, patient's race or ethnic group may assist in differential diagnosis. Other superficial skin conditions such as: psoriasis, atopic dermatitis, tinea capitis may be confused with seborrheic dermatitis. Distinguishing severe seborrheic dermatitis from early facial psoriasis is usually difficult. Diagnosis is based on direct microscopic examination of skin scrapings in KOH. Skin biopsy is used to rule out cutaneous lupus erythematosus (Berk & Scheinfeld, 2010).

***Malassezia* folliculitis**

This is based on clinical findings and response to therapy. However, microscopy of material scraped from pustules can be helpful when the diagnosis is unclear. One may scrape a pustule with a No.15 blade; spread the expressed material on a slide; and treat with potassium hydroxide, Swartz Lamkins, or Chlorazol black E dye before viewing by microscopy. Budding yeast are the characteristic finding. This is in contrast to pityriasis versicolor, also caused by *Malassezia* yeasts, but which shows pseudohyphal forms (Levin, 2018). Fungal culture is seldom used in the diagnosis of *Malassezia* folliculitis, because the causative yeasts do not grow on standard mycology media. Culture is best on media containing olive oil or another lipid source (Levin, 2018).

Histopathology of skin biopsy shows dilated follicular openings with keratin plugging, cellular debris, and a mixed inflammatory infiltrate. Special fungal stains may highlight budding yeast forms and spores within the follicle (Levin, 2018)

Atopic dermatitis

Features used in the Western world vary with ethnicity and genetic background, it only aid diagnosis. African dermatologists have reservation on the Hanifin criteria for the diagnosis of atopic dermatitis and the need to improve on it for African use (Nnoruka, 2004).

There are no known or reliable biomarkers that can distinguish atopic dermatitis from other conditions. The diagnosis is based on the signs, symptoms and patients history (Eichenfield *et al.*, 2014).

Psoriasis

There are different clinical types of psoriasis (Canadian Psoriasis Guidelines Committee, 2009). Chronic plaque psoriasis presents as well-demarcated erythematous symmetric plaques with overlying silvery scale on the scalp, trunk, buttocks, and extremities. The isomorphic type occur on previously normal skin that has sustained trauma or injury (Whan *et al.*, 2017). Careful observation and skin biopsy might be helpful in diagnosis (Whan *et al.*, 2017).

Modalities for treatment of *Malassezia* infections

a. Pityriasis versicolor

Treatment of pityriasis versicolor could be topical or systemic or the combination of both. Topical medications include: Sulphide (2.5%), Sodium thiosulphate with 1% salicylic acid, 50% propylene glycol in water, zinc pyrithione shampoo, 0.1% ciclopirox solution and topical azoles (1% clotrimazole, 1% bifonazole and 2% ketoconazole) (Nura *et al.*, 2016). Systemic medications are with azoles which should be administered with caution because of the side effects. Ketoconazole, Itraconazole and Fluconazole are drugs of choice (Nura *et al.*, 2016).

b. Seborrheic dermatitis

The treatments of seborrheic dermatitis consist of antifungal agents, immunomodulators, corticosteroids and Keratolytics. Their mode of action are; inhibition of skin colonization, dissolving of the scales and crust, itching and inflammation reduction (Gary *et al.*, 2015).

Tea tree oil shampoo can also be used to decrease symptoms of mild infections (Sanfilippo and English, 2006). For long-term control, antifungal shampoos can prevent relapse (Kircik, 2010). Severe scalp inflammation may be treated with topical corticosteroids such as hydrocortisone and beclomethasone dipropionate. This treatment is expensive and associated with adverse effects (Gary *et al.*, 2015). The use of hair creams containing groundnut oil may enhance seborrheic dermatitis. Biobelemony *et al* (2016) reported that

groundnut oil enhances the growth of *Malassezia* species and should not be used in the preparation of hair ointment or creams.

c. Atopic dermatitis

The treatment of atopic dermatitis involves systemic therapies in combination with sedating antihistamine and time-consuming phototherapy (Sidbury *et al.*, 2014). Systemic corticosteroids are in general not ideal for the treatment of atopic dermatitis (Silverberg, 2014; Naygaard *et al.*, 2017).

d. Malassezia folliculitis

Oral therapy includes: Fluconazole 100-200mg daily for 2-3 weeks, and 200mg once monthly for maintenance. Itraconazole 200mg daily for 7 days, and then 400mg once monthly for maintenance. Isotretinoin 1mg/kg/day for 16-20 weeks for recalcitrant case.

Topical therapy is recommended as an adjunct to oral therapy, not as monotherapy. Ketoconazole 2% lotion can be applied daily, followed by 2% ketoconazole shampoo used 2-3 times weekly for maintenance. Others include daily application of 1% Econazole nitrate cream, 1% Clotrimazole cream, and 1% Ciclopirox olamine solution. Also, 1% Selenium sulfide or 2.5% shampoo and body wash can be used once weekly.

e. Psoriasis

Topical and systemic therapy is used (Whan *et al.*, 2017). Corticosteroid is considered the cornerstone of topical treatment for patients with mild psoriasis (Menter *et al.*, 2009). Although uncommon, long-term use of corticosteroid results in side effects such as tachyphylaxis, hypothalamic-pituitary-adrenal axis suppression and local skin changes (Canadian Psoriasis Guidelines Committee, 2009).

Vitamin D3 analogues can be used for the treatment of plaque and severe scalp psoriasis. The analogue acts by inhibiting T lymphocyte activity and keratinocyte proliferation (Whan *et al.*, 2017).

II. Material And Methods

A narrative approach was adopted for this review. Studies published in English between January 1990 and October 2018 was included in the review. This review made use of documented findings from previous works using multiple data base consultation for literature including PubMed, MEDLINE, Google scholar, and Cochrane database search.

III. Discussion

Over the years, research has shown that *Malassezia* species are responsible for pityriasis versicolor, *Malassezia* folliculitis and other *Malassezia* diseases. They act as an exacerbating factor in atopic dermatitis seborrheic dermatitis as well as psoriasis (Sugita *et al.*, 2010; Saunders *et al.*, 2012).

This review showed that pityriasis versicolor had the highest prevalence in Malawi where 17.9% of the studied population had mild and extensive form of the disease followed by Central African Republic (16.6%) while Mali (1.6%) had the least prevalence. The lesions were more common on the face than other sites as reported by Akpata *et al* (1990) and Bélec *et al* (1991) in Cross River State, Nigeria and Central African Republic respectively. The disease was more common in people aged 12-16years. This is because the disease occurred in adolescents with high sebaceous gland activity (Theodore *et al.*, 2014). The treatment of pityriasis versicolor can be carried out topically or systemically or the combination of both using several kinds of antifungal agents and/or topical azoles. However, the use of a combination therapy is often recommended for more effective results.

The prevalence of seborrheic dermatitis in Abakili, Nigeria in the study of Okoh *et al* (2018) was higher than the other African countries where such studies were conducted. These countries are: Ghana, Gabon and Rwanda where the disease occurred more in infants and adolescents. The limited reports on the prevalence of seborrheic dermatitis may be due to the absence of validated diagnostic criteria and lack of attention to the disease.

This study also reported that atopic dermatitis had its highest prevalence in Côte d'Ivoire (9.2%) (Ahogo *et al.*, 2017) followed by Nigeria (8.4%) (Nnoruka, 2004), while least prevalence (0.65%) was reported in Tunisia (Amouri *et al.*, 2011).

Cases of psoriasis has been proven among individuals in Africa including West and East Africa. Nnoruka (2005) reported 2.6 to 3.3% prevalence in East Africa (Kenya, Uganda and Tanzania) while Ayanlowo and Akinkugbe (2016) reported 1.13% prevalence in Nigeria. These prevalence differences can be attributed to climate especially sunlight that would have a moderating effect on the expression of the disease but with regional variances related to climate and genetics (Ayanlowo and Akinkugbe, 2016).

IV. Conclusion

Malassezia skin infection is a health problem in different parts of Africa. Topical and systemic antifungal agents is the most commonly modalities for the treatments of these diseases. There is need for improvement in diagnostic techniques for these conditions.

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