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Superficial Mycosis in HIV Positive Patients

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Abstract

Introduction: The incidence of superficial mycosis in patients with human immunodeficiency virus (HIV) is increasing in India. *Aims and objectives*: 1. To determine the prevalence, clinical variations, common aetiological agents of superficial mycoses and its CD4 count in HIV-positive subjects in our area. *Methods and Material*: A study was carried out among 150 HIV positive patients over a period of 18 months. Clinical observations were followed by conventional laboratory methods for diagnosis of aetiological fungal species. *Results*: The number of patients 62/150 (41.3%) had at least one superficial mycosis. Dermatophytosis (64.71%) was the commonest presentation followed by onychomycosis (26.47%). The two sites involvement was seen in 9.67% followed by (2.94%) patients each with extensive tinea corporis and tinea versicolor. The fungal species isolated were *T. rubrum (35.29%), T. mentagrophyte* (10.29%), *T. verrucosum* (2.94%), *T. tonsurans* (2.94%), *T. schonlenii* (1.47%) and *M. canis* (1.47%). Non-dermatophytes identified were *Candida* spp. (8.82%), *Scopulariopsis* spp. (5.88%), *Fusarium* spp. (1.47%) and *Malassezia* spp. (2.94%). Only one isolate of *Sporothrix sckenskii* was isolated. Statistical analysis : by using statistical package for social sciences (SPSS) software. *Conclusions*: In majority of patients, the clinical presentations did not differ from those found in immunocompetent individuals. We found nondermatophytic onychomycosis and atypical presentations which is rare in immunecompetent patients. We found no increased incidence of superficial mycosis with decreased CD4 count.

Keywords: CD4 Count; HIV; Superficial Mycosis.

Introduction

There is an increased incidence of superficial mycosis among various cutaneous dermatoses, in HIV positive patients. These are extensive, atypical and resistant to the conventional treatment [1,2,3]. also inverse relation with CD4 counts [4]. An Indian study has shown 42% prevalence rate of mycotic skin infections in HIV positive patients [5]. The global variations in the incidence are due to change in climatic conditions, lifestyles, local variations in pathogens and socioeconomic data [6]. Therefore the present study undertaken to know the magnitude of this problem in our area. This will help clinician for correct diagnosis and treatment [7] which improves prognosis.

Material and Methods

The present study was carried out in 150 HIV seropositive patients, attending the ART centre at our tertiary care hospital after the ethical approval from

institutional ethical committee. The clinically diagnosed cases of superficial mycotic infections (involves skin, hair, nail and mucosa) were recruited for this study.

Inclusion Criteria

All HIV positive patients attending ART centre.

Exclusion Criteria

Clinically diagnosed cases of bacterial or viral skin infection, cutaneous drug eruption and systemic mycosis.

Detailed history and informed consent from each patient was recorded in the case report form. The following investigations were done:

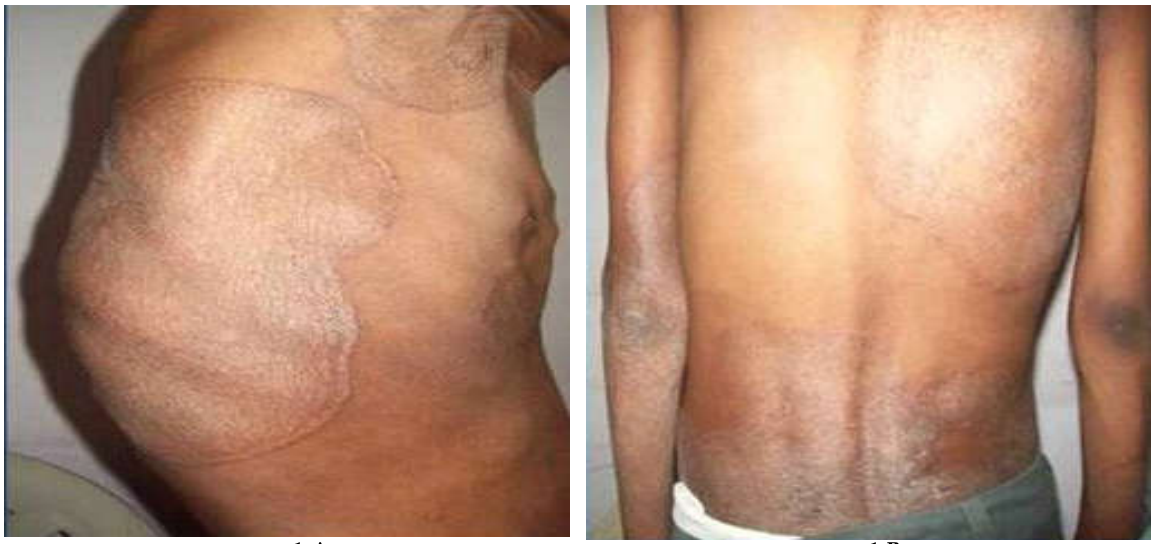
1.CD4 estimation:- By Flow cytometry (BD FACS Caliber micro bead based system.) The most recent CD4 count of the patient was used for analysis.

2. For confirmation of fungal etiology of superficial mycosis: After clinical observations, samples were collected from skin (scraping with scalpel), nails (debris under nail/ affected part of nail clipping), hair (by plucking), pus and mucosa (either swab or scraped with blunt scalpel) as appropriate [31]. The sample was used for inoculation of culture media and direct microscopy (10% KOH). (For nail- 20% KOH in sterile bulb overnight) Findings were noted in KOH mount. Fungal culture was done on Sabouraud's dextrose agar (Emmon's modification) with chloramphinicol and DTM (Himedia Pvt Ltd). Incubation, gross examination of fungal colony characteristics and microscopic examination of cultures by lactophenol cotton blue preparation was done as per standard guidelines [31]. Culture with negative reports were repeated in highly suspicious clinical cases as false negative results are known to occur in almost one third of the cultures [3].

In cases where speciation was difficult slide culture was done for mould identification. In addition, tests were done for identification of fungal isolate as dermatophytes which includes thermotolerence tests, urease test, healthy hair penetration test, rice grain test. Tests were done for confirmation of thermal dimorphism in case of dimorphic fungi (i.e yeast form and filamentous form of the fungus were demonstrated at two different temperature i.e 25^0C and 37^0C respectively.) The germ tube test was used to identify Candida albicans. In addition to slide culture, Hichrome candida differential agar, sugar assimilation pattern was used for speciation of candida spp. In cases of tinea versicolor, sterile olive oil was added to the culture medium [31].

Observations and Results

A total of (62/150) 41% were clinically diagnosed as superficial fungal infection. Of which 51/62 (82.18%) were males and 11 (17.82%) were females hence the ratio was 4.6:1. Subjects were between 7-65 years of age hence the mean age was 35.66 + 10.72 years. In our study, (75.8%) men were employed (48.38% in unskilled & 22.58% in skilled) and (4.84%) of females were employed. Most patients 49/62 (79.03%) were in early stage while 13/62, (20.96%) were in stage IV of HIV infection. The duration of



1 A **1 B**

Fig. 1: Extensive Tinea Infection (Fig. 1A,1B: shows involvement >30% body surface area)

symptoms > one year, six to twelve months, <six months was observed in (41.9%), (22.5%) and (35.4%) patients respectively. There was no predisposing factor such as constant irritation, excessive sweating, trauma etc in majority (45.09%) patients.

Dermatophytosis 44/68 (64.71%) was the most common clinical presentation followed by onychomycosis 32/68 (47%). Out of six (9.67%) two site involvement cases, two patient had toe nail onychomycosis with tinea cruris, one patient had finger nail onychomycosis with tinea pedis, two patient had finger nail onychomycosis with mucocutaneous candidiasis and one patient had tinea corporis with mucocutaneous candidiasis. Cases of extensive tinea corporis (2.94%) (Figure 1), atypical cutaneous sporotrichosis involving right temporal aspect of the scalp in thickened, crusted form with matted hairs which was misdiagnosed as tinea capitis (Figure 2A), superficial mycosis involving external genitalia (scrotum, groin) (Figure 2B), mucocutaneous candidiasis (5.88%) and tinea versicolor (2.94%) were seen. Toe nail and finger nail were affected in 24/68 (35.29%) and 8/68 (11.76%) respectively. The type of most common onychomycosis was Distal and Lateral Superficial Onychomycosis (DLSO) type (81.24%), followed by Proximal Superficial Onychomycosis (PSO) (9.37%) (Figure 2C), Candidial paronychia (6.25%) and Total Dystrophic Onychomycosis (TDO) (3.12%)(Figure 2D).

2 A 2B 2C 2D

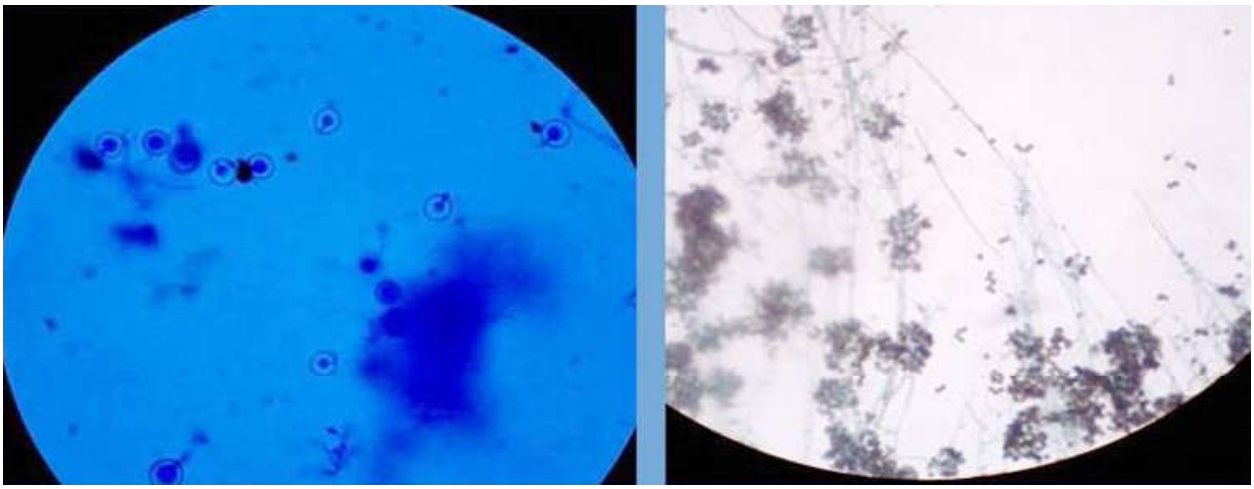
Fig. 2: Atypical superficial mycosis and types of onychomycosis **(**Fig. 2A: Shows thick, crusted plaque with matted hairs on Right Temporal area of scalp, Fig. 2B: Shows T. Cruris with involvement of scrotum, Fig. 2C: PSO, Fig. 2D: TDO**)**

3 A 3B

Fig. 3: Culture on SDA (non dermatophytes and dimorphic fungi) Fig. 3A: (*Scopulariopsis spp.)* after 25 days Obverse: Whitish to pink, powdery; Reverse: cream to brownish colored. Fig.3B: (*S. schenckii*) after 30 days Obverse: grey brown to black velvety.

Table 1: Involved body site and isolated fungal species (n=68).

Involved body site	Isolated species	No. of isolate	Involved body site	Isolated species	No. of isolate
Skin and mucosa (n=36)	*T. rubrum*	13	Nail (n=32)	*T. rubrum*	11
	T. mentagrophyte	2		*T. mentagrophyte*	5
	T. tonsurans	1		*T. verrucosum*	2
	M. canis	1		*T. tonsurans*	1
	C. albicans	3		*T. schoenlenii*	1
	C. kruzii	1		*C. albicans*	1
	Malassezia spp.	2		*C. kruzii*	1
	Sprothrix schenskii	1		*Scopulariopsis spp.*	4
	No growth	9		*Fusarium spp.*	1
	Contaminants	3		*No growth*	4
				Contaminants	1
		24			27
		Total =	**51/68**		



4 A **4B**

Fig. 4: LCB findings. Fig. 4A: *(Scopulariopsis spp.)* septate hyphae, conidiogenous cell on undifferentiated hyphae. Conidia are one-celled, spherical, 5 x 7µm. Fig. 4B: (*Sporothrix. schenckii*) Slender hyphae, sporulation- 1. Spore on delicate sterigmata along hyphae and 2.pyriform spores in groups; (flower like pattern)

Superficial mycosis involved skin 36/68 (58.08%), nail 32/68 (51.56%) and hair (0%). Six patients had two site involvement i.e 12/68 (17.64%). Dermatophytes 37/68 (54.41%) and non dermatophytes 14/68 (20.58%) were isolated. The KOH mount findings were positive (66.16%) and negative (33.82%). Among all fungal cultures; the results were pathogenic fungi (75%), no growth (19.12%) and contaminated (5.88%). Samples were found positive (60.29%) and negative (16.17%) by both KOH and culture, (17.64%) by culture alone, (5.88%) by KOH alone.

All dermatophytes (n=37)were grown on SDA 37/51 (72.55%) while 29/51 (56.86%) on DTM. The dermatophytes isolated were *T. rubrum* (35.29%) followed by *T. mentagrophyte* (10.29%), *T. verrucosum*(2.94%), *T. tonsurans* (2.94%), *T. schoenlenii* and *M. canis* (1.47%) each. Nondermatophytes isolated were *Candida spp.*(8.82%), *Scopulariopsis spp.* (5.88%) (Figure 3A & 4A), *Fusarium spp.* (1.47%) *and Malassezia spp.* (2.94%). The non-dermatophyte fungi as pathogen had been confirmed by: a) KOH mount Positive 2) Repeated isolation (twice). 3) Immunosupressed state, as used in study by Surjushe Amar et al [12]. Colony morphology on SDA and LCB findings were suggestive of *S. schensckii* (Figure 3B, & 4B) in suspected case of tinea capitis. The findings of samples as culture negative and contaminents were seen in 25% and 5.88% patients.

Mean CD4+ cell count was 288.85/µL. Majority (40.32%) patients had CD4 count between 300 - 700/µl while in (20.96%) patients CD4 count was 201 - 300/µl. The CD4 cell count was between 101 - 200/µL (in 16.12% patients) and 51-100cells/µl (in 11.29% patients). Five subjects (8.06%) had CD4 cell count <50/µL.

Discussion

With the advent of HAART, the course of HIV has changed and also associated dermatological lesions (Maurer and Lori 2004). The prevalence of cutaneous fungal infection was (41.3%) of which 75% cases were confirmed by mycological examination. From India, similar findings had been noted by Kadyada Puttaiah Srikannth et al [5]. (42%). Torssander J et al [8] and Aly R and Tmothy Berger [9] also observed the same (37%).

Majority of our cases of superficial mycosis were seen in the early stage of HIV infection. Kaviarasan PK et al [10] and Rosatelli et al (17% in stage IV HIV patients) and Singh A et al (32.9%), as having similar findings. The age group (21-40 years) predominantly affected. Same age group was affected in study by J Lohoue petmy et al [11] and V Satya Suresh Attili et al [6] Majority of the male (75.8%) and females (4.84%) were employed in unskilled occupation. Kadyada Puttaiah Srikannth et al (48%) 5 and Kaviarasan PK (46%) [10] had also noted same. In our study trauma (20.9%) (in onychomycosis cases) was the commonest predis-posing factor, followed by excessive sweating 12.9%, constant irritation/ occlusion 9.6%, malnutrition 4.8%, continuous immersion of hand in water 3.2% and PVD 1.6%. Surjushe Amar et al [12] had noted trauma 46.66%, Diabetes mellitus 10% and PVD 1.66% as predisposing factors in cases of onychomycosis.

Dermatophytosis

The prevalence of dermatophytosis in our study is 44/150 (29.33%), Kaviarasan PK et al [10] and Di Silverio A at al [13] had similar findings. Kumarasamy N (8%) [2] and Sharma Y K et al (8.33%) [14] noted lower prevalence rate. Tinea unguim (17.74%), tinea corporis (16.12%), tinea cruris (14.72%) was common presentations. Torssander J et al [8] found tinea pedis as the commonest dermatophytosis. Kaviarasan PK et al [10] found 53% tinea corporis, 49% tinea cruris, 7% tinea pedis, and 24.4% tinea ungium cases. These findings showing higher number of patients with mycotic skin infections, may be due to involvement of the HIV stage IV patients [10].

Two case reports of extensive tinea infection (3.22%) was found in our study. D. Craig Wright et al [15] and Goodman DS et al [16] had also reported extensive spreading tinea infection among HIV positive individuals. Study by Kaviarasan PK et al [10] noted 22.8% cases of extensive tinea infection which may be due to HIV group IV study subjects. Dermatophytosis involving penis and scrotum were noted. In a study by Aly R and Tmothy Berger [9]. findings as dermatophytes involving the external genitalia were noted. (a rare site affected in dermatophytosis cases)

Clinically 24/150 (16%) patients were diagnosed with non dermatophytic skin infection. Only a few case reports were available on non dermatophyte causing dermatomycosis [17,18]. The prevalence of onychomycosis was 32/150 (21.33%). We found toe nail (35.29%) and finger nail (11.76%) onychomycosis, similar to the findings of Surjushe Amar et al [12] and Aly R and Tmothy Berger [9]. The frequency, sequence of different types of onychomycosis was same as in study by Surjushe Amar et al [12] and Gupta AK et al [19].

Onychomycosis due to nondermatophytes : Clinical clues used- 1.The absence of T. pedis. 2. Only toe nail affection. 3. History of trauma. 4. non responsiveness to systemic antimycotics. 5. periungual inflammation. Similar clues were used in literature [15]. Majority 18/68 (20.58%) patients had fulfilled the above criteria. Three cases 3/68 (4.41%) of PSO were found in our study. Similar findings were seen in studies by Surjushe Amar et al [12], R Kaur et al [17] and Kaviarasan PK et al [10]. The reason of preponderance of proximal onychomycosis in HIV is unknown [17]. A total of candidial infections 6/68 (8.82%) were seen in our study. The lower number of candidial infections in our study may be due to following reason: 1.The patient selection bias as we have taken patient on ART and not pre ART. 2. OPD rather than IPD patient 3. asymptomatic patients 4. cutaneous *Candidiasis* per se is uncommon.

Tinea versicolor was found in 2/68 (2.94%) cases. No case of tinea versicolor seen in Kadyada Puttaiah Srikannth et al [5]. J Lohoue petmy et al (10.52%) [11], Di Silverio A et al (25%) [13] and D. Craig Wright et al (25%) [15] had seen higher number of tinea versicolor cases. The difference may be due to geographical, climatic variation, asymptomatic patients and HAART. We report a case of cutaneous sporotrichosis 1/68 (1.47%) which was misdiagnosed as tinea capitis. This was an atypical presentation. In India, sporotrichosis is found endemic in few northern states in non HIV populations [26].

T. rubrum (35.29%) was the commonest fungus isolated. This is same as in studies by J Lohoue petmy et al [11] and Kaviarasan PK et al [10]. The other dermatophytes received only a meagre onus of the infections 13/68 (19.11%). Similar findings were noted in the study by Graham E. J. Rodwell et al [20]. We found single case of tinea corporis where *M. canis* was isolated. Bournerias I et al [21] also noted that *M.*

canis was relatively rare even in HIV infected cases. No subject in our study, was infected with *Epidermophyton* spp.. Study by Graham E. J. Rodwell et al [20] also had similar findings. The non dermatophytes were isolated in 14/68 (20.58%); *Scopulariopsis spp., Fusarium spp.*, (& *Candida* spp., *Malassezia* spp.) Similar finding noted by J Lohoue petmy et al [11]. An increasing incidence of non dermatophytic species are on rise in patients with HIV [18]. Speciation holds therapeutic impact [22].

Onychomycosis

We found dermatophytes (62.5%) and non dermatophytes (21.87%) as a causative agent. Ravnborg L et al [23] found dermatophytes more prevalent while Cribier B et al [24] as nondermatophytes. We found *Scopulariopsis* spp. 4/68 (5.88%), *Fusarium* spp. 1/68 (1.47%) as rare isolate. Dompartin D et al [25] had *found 4% Scopulariopsis* spp. And Kedma de Magalhaes Lima [102] and J Lohoue petmy et al[11] had isolated *Fusarium* spp.

Mean CD4 count was 288.85/µl, as in the study by Sharma Y K et al [14] and V Satya Suresh Attili et al [6]. Dermatophytic infections were clustered between 300-700cells/µl. This is in concordance with published literature [27]. The cases of superficial mycosis were not increased with decreased CD4 count. This is also seen in studies by Kumarasamy N et al [2] and Graham E. J. Rodwell et al [20]. Brig Y K Sharma [14] also stated that dermatophytes cannot be taken as AIDS defining illness per se.

Extensive form, atypical presentations and proximal onychomycosis were observed when CD4 count was 50 - 200cells/µl. Out of six cases of fungal infections involving two sites on presentation, two had CD4 counts < 200/µl. Similar findings were observed by Sharma Y K [14] and D. Craig Wright et al [15].

Majority cases of onychomycosis had CD4 count >300 cells/µl. Conant MA et al [28] stated as 450cells/ìl. Tinea versicolor cases were seen between 700 - 1000cells/µl. Patients with cutaneous sporothrix infection had CD4 count 127cells/µl. It was 91 cells/µl by Raquel Vilela et al [29] and 30cells/µl by S. Hardman et al [30].

In the view of these results, emphasis should be placed on the systematic examination of skin in all HIV infected patients. Hence advice regarding the simple preventive measures prevents the recurrence and improves prognosis. This affects the patient's quality of life. Although conventional mycological techniques take a long time (2 - 4 weeks) to identify the fungal isolate, they still hold promise for diagnosis [3,10]. Limitations of the study- there could be subjective differences in interpretation of results but these are minimal. The confirmation of fungal isolate was done with the help of available resources which had been tried to nullify with the help of slide culture. We have not included stage IV HIV patients, hence correlation with CD4 may be affected. We have not done antifungal sensitivity testing for filamentous fungi as the fungi isolated from these group of patients may be resistant to conventional treatment [3]. Hence further research are needed in this arena.

Conclusion

From this study it can be concluded that mycotic skin infections due to dermatophytes were common in HIV positive patients. Atypical presentations such as scrotal and penis involvement by dermatophyte were seen in HIV positive patients. *T. rubrum* was the commonest species. The non dermatophyte especially *Scopulariopsis* spp. as a cause of onychomycosis is an emerging pathogen. Single case reports of infection caused by *Fusarium* spp., *M. canis and S. schenckii* each, points out their emerging pathogenic potential in HIV patients. Most of the fungi causing mycotic skin infections have found as clustered between 100 to 700 cells/µl. This clustering may be due to involvement of only OPD patients on HAART. There was definite correlation between extensive tinea infection, superficial mycosis involving two sites and pathognomic lesion of AIDS such as PSO with CD4 count 50-200/µl.

Key Messages

The presence and importance of Extensive tinea infection, Atypical dermatophytosis, fungal infections involving two sites as well as non-dermatophyte as a causative fungus should be considered in HIV patients as CD4 count decreases.

Abbreviation

DTM: Dermatophyte test medium,

HAART: Highly Active Anti-retroviral Therapy,

HIV: Human Immunodeficiency Virus,

KOH: Potassium Hydroxide,

LCB: Lactophenol cotton blue,

NACO: National

AIDS Control Organization,

NDM: Non Dermatophytic, P

VD: Peripheral Vascular Disease.,

SDA: Sabaroud's Dextrose Agar, Spp.: Species.]

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