Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/mjafi

Original Article

A comparative study of the various patterns of oro-cutaneous fungi and their sensitivity to anti fungals between HIV patients and normal healthy individuals

Lt Col P. Vijendran^{a,*}, Brig R. Verma^b, Col N. Hazra^c,
Col B. Vasudevan^d, Wg Cdr M. Debdeep^e, Lt Col V. Ruby^f,
Maj N. Shekar^g

^a Classified Specialist (Dermatology and Venereology), Base Hospital, Lucknow 226002, India

^b Commandant, Base Hospital, Lucknow 226002, India

^c Senior Advisor (Microbiology), Command Hospital (Central Command), Lucknow 226002, India

^d Senior Advisor (Dermatology and Venereology), Base Hospital, Lucknow 226002, India

^e Graded Specialist (Dermatology and Venereology), Base Hospital, Delhi, India

^f Graded Specialist (Dermatology and Venereology), Command Hospital (Southern Command), Pune 411040, India

^g Graded Specialist (Dermatology and Venereology), Command Hospital (Eastern Command), Kolkata 700021, India

ARTICLE INFO

Article history:

Received 10 October 2016

Accepted 15 January 2018

Available online 5 March 2018

Keywords:

Oro-cutaneous fungi

Fungal resistance

Dermatophytes

Atypical fungi

HIV/AIDS

ABSTRACT

Background: Dermatological diseases are the first recognized clinical manifestation Human Immunodeficiency Virus (HIV) and Acquired Immune Deficiency Syndrome (AIDS).^{1,2} The present study was undertaken to find out the clinical spectrum of the superficial mycoses, the etiological organisms and their drug sensitivity patterns among HIV positive patients and non HIV individuals attending the tertiary care hospital.

Methods: The study population was 100 HIV patients and control patients were consecutive 100 HIV negative patients. Skin scrapings and swabs were obtained from the upper back, web spaces of toes, inguinal region, dorsum of tongue. All the samples were subjected to potassium hydroxide mount and stained with Calcoflour White and were cultured. The fungi were identified on the basis of colony and microscopic features in conjunction with results of physiologic evaluation by standard phenotypic identification criteria.

Results: The total number of seropositive patients who had atleast one fungal infection was 57 and the total number of seronegative patients who had atleast one fungal infection was 21. In our study, fungal colonization was seen in 3.6% in clinically normal sites in retro-positive patients and 1.6% in retronegatives. 76.59% in retropositive and 85.71% in retronegative patients the fungi cultured were sensitive to fluconazole.

* Corresponding author.

E-mail address: vijendranpria@yahoo.co.in (P. Vijendran).

<https://doi.org/10.1016/j.mjafi.2018.01.004>

0377-1237/© 2018 Published by Elsevier B.V. on behalf of Director General, Armed Forces Medical Services.

Conclusion: The findings of this study suggest that the skin of HIV patients may more frequently harbour common fungi even in the absence of visible clinical signs. Antifungal-resistant fungi should be kept in mind while treating fungal infections.

© 2018 Published by Elsevier B.V. on behalf of Director General, Armed Forces Medical Services.

Introduction

Human Immunodeficiency Virus (HIV) is a retro-virus that compromises the cellular immune system of the body making it susceptible to fungal infections. Dermatological diseases, in particular superficial fungal infections are the first to be detected and are seen at every stage of HIV infection and often are the presenting feature. They often are the clue towards underlying HIV infection.^{1–3} Superficial fungal infections are the most common and one of the earliest oro-cutaneous markers of infective conditions to occur in the HIV/AIDS patients.⁴ Majority of fungal infections are caused by organisms that are part of the normal flora of the individuals. Apparently healthy skin of immunocompromised patients showed a higher incidence of fungal presence in apparently normal looking skin.^{5,6} Determining fungal flora assumes importance because of the role of skin as reservoir in causing infections in the highly susceptible HIV/AIDS patients. Several studies suggest an impairment in a number of host defense mechanisms in persons with HIV infection such as salivary flow rates, condition of the epithelial barrier, antimicrobial constituents of saliva, presence of normal bacterial flora, and local immunity.^{7,8} Dermatophytes infect skin, nails and hair, colonize in keratin. Invasion of the epidermis with dermatophytes requires adherence between arthroconidia and keratinocytes possibly resulting from enzymatic action. Dermatophytes invoke the development of a host response that depends on both innate and acquired immunity. Cellular immunity via development of sensitized lymphocytes is a key factor in immunological response, thus chronic infections are seen with poor T lymphocyte response.⁹

In endemic areas, a variety of fungi like *Aspergillus*, *Fusarium*, *Histoplasma*, *Coccidioides*, *Exophiala jeanselmei*, *Phaeoconium lilacinum* have caused cutaneous manifestations in immunocompromised individuals.^{10,11} In a healthy individual, infection is typically self-limited, although latency is commonly established, rather than elimination. Reactivation of latent infection may subsequently occur if the infected individual becomes immunosuppressed.^{12,13} Primary infection or reactivation in individuals with impaired immune surveillance presents a different scenario in which the disease may continue as a locally invasive process. These factors indicate that under immune suppressed conditions there is an imbalance of cell-mediated immunity in immune compromised skin as seen in HIV/AIDS cases, the commensals colonizing certain sites become a pathogen and cause clinically apparent infection. The present study was undertaken to compare the colonization and clinical spectrum of

the superficial mycoses in clinically affected lesions, the etiological organisms, and drug sensitivity patterns among retro positives and retro negatives attending the tertiary care centre.

Materials and methods

The study population in this prospective study was serving Armed Forces personnel admitted in a tertiary care centre. Institutional ethical clearance was obtained. The sample size was calculated with the following specifications: Level of significance (α) = 5%, Power = 80%. The sample size was calculated based on the available independent studies showing the prevalence of superficial mycoses in HIV and non HIV patients. The following specifications were assigned: Level of significance (α) = 5%, Power = 80%. One study with sample size of 97, showed *Candida* with proportion for 60% in HIV cases and 40% in non HIV individuals. Another study with a sample size of 79, recorded proportion of dermatophyte infection as 30% for HIV and 12% for non HIV cases. Hence sample sizes of 100 cases each were chosen in study group and control group. Dermatology perspective One hundred consecutive HIV patients (all male) admitted in immune deficiency centre of tertiary care hospital and 100 non HIV persons (all male) admitted in dermatology and leprosy ward acting as controls were subjected to a thorough history and clinical examination. Among the controls those with diabetes, immunosuppressive drugs, and malignancies were excluded. Skin scrapings and swabs from these patients were obtained from upper back, web spaces of toes, inguinal region, and dorsum of tongue.

All the samples were mounted in 10–30% potassium hydroxide mount and stained with Calcoflour white and examined under direct and fluorescent microscopy. Gram's stain was also carried out on direct scrapes for *Candida* infections. The samples were cultured in Sabouraud's Dextrose agar, Mycobiotic agar and Dermatophyte test medium. The microscopic examination of fungal growth was observed with lactophenol cotton blue stain after a slide culture mount was prepared. The dermatophytes were identified on the basis of colony and microscopic features in conjunction with results of physiologic evaluation by standard phenotypic identification criteria. *Candida* species were identified on the basis of germ tube production, spore formation in corn meal agar and sugar assimilation tests (Fig. 1). The fungal isolates were subjected to anti fungal sensitivity/resistance testing by disc diffusion and E-tests. Susceptibility testing was performed as per CLSI (Clinical and Laboratory Standards Institute) stan-

Fig. 1 – (a) Chronic pseudomembranous candidiasis on tongue. (b) Candidal balanoposthitis. (c) Gram's staining of candida showing yeast cells and pseudohyphae. (d) Cream coloured colonies of *Candida* on Sabouraud's agar. (e) Germ tube test showing hyphal extension of yeast cells confirming *Candida albicans*.

Table 1 – Age wise distribution.

Age range (in years)	No of retropositive cases	Retropositive with fungal infection (n = 100)
0-20	02	00
21-40	83	47
41-60	15	10
Total	100	57 (57%)
Age range (in years)	No of retronegative cases	Retronegative with fungal infection (n = 100)
0-20	10	02
21-40	74	14
41-60	16	05
Total	100	21 (21%)

dards (M27-A3 and M38-A2). Broth microdilution methods was performed for yeasts and filamentous fungi isolates. Stock solutions was prepared in sterile water for watersoluble antifungal powder and dimethyl sulfoxide for water insoluble antifungal powder. Further serial two fold dilutions were performed in RPMI 1640 medium, using flat-bottomed 96-well microdilution trays. The tabulation and interpretation of the results was based on the objective proforma illustrating the above sites. Standard univariate and bivariate analysis was applied for interpreting the data. Z test (to compare between

two proportions) and Fisher's exact test and Chi-square test by Yate's correction was used.

Results

The total number of HIV positive patients (n = 100) who had at least one fungal infection was 57 and the total number of Non-HIV individuals (n = 100) who had at least one fungal infection was 21. The age group of 21-40 years was most commonly involved in both the groups (Table 1).

Microbiological perspective: Fungal positivity (denote either KOH positivity or culture positivity) in HIV Positive Patients and HIV Negative Individuals. A total of 42 samples were positive for fungus in KOH mount and a total of 27 samples yielded positive culture. Among the total 42 samples which were positive for fungus in KOH mount, 18 were found to be culture positive as well (p-value < 0.001 and odds ratio 37.41 with a CI of 15.22-91.97). The maximum fungal positivity (KOH + Culture) was yielded from dorsum of tongue (37) followed by the web spaces of the toes (Table 2a). A total of 24 samples was positive for fungus in KOH mount and a total of 14 samples yielded positive culture in HIV negative individuals (Table 2b). Among the total 24 samples which were positive for fungus in KOH mount, 8 were found to be culture positive as well (p-value < 0.001 and odds ratio 39.16 with a CI of 12.15-

Table 2a – Microbiological examination in retropositive individuals from normal sites. Total of 500 samples were taken from normal sites (5 sites × 100 patients).

	Culture +ve	Culture –ve	Total
KOH +ve	18 (3.6%)	24 (4.8%)	42
KOH –ve	9 (1.8%)	449 (89.8%)	458
Total	27	473	500

Table 2b – Microbiological examination in retronegative individuals from normal sites.

	Culture +ve	Culture –ve	Total
KOH +ve	08 (1.6%)	16 (3.2%)	24
KOH –ve	06 (1.2%)	470 (94%)	476
Total	14	486	500

126.18). The maximum fungal positivity (KOH + Culture) was yielded from dorsum of tongue (14) followed by the web spaces of the toes (7).

A total of 500 samples each were taken from normal sites in retropositive and retronegative individuals, KOH and culture results are as shown in (Tables 2a and 2b).

Correlation with CD 4 count: Maximum number of fungal infections were noted in the group with CD4 count < 200 cells/μl, the percentage of patients affected being 77.77%. Fifty percent of patients with CD4 count in the range of 200–499 cells/μl had fungal infections, whereas 28% patients with CD4 count > 500 cells/μl had fungal infections. Candida infection was commoner in patients with CD4 count range of 200–499 and <200 (Table 3).

Species characteristics: The most common superficial fungal infection encountered among the HIV positive patients were various forms of candida infections, accounting for 63% of the total infections, whereas dermatophytes were the most common fungal infectious agent among HIV negative individuals, accounting for 61.9% of total infections (Tables 4a and 4b).

Candida albicans was the only candida species grown among HIV negative individuals whereas they constituted 80.55% among the HIV positive patients, the remaining 19.45% being non *albicans* candida species. Only *Trichophyton rubrum* (69.23%) and *Trichophyton mentagrophytes* (30.76%) were grown among HIV negative individuals whereas others like *Trichophyton tonsurans* (13.63%) and *Epidermophyton floccosum* (4.54%) were also grown among HIV positive patients along with *T. rubrum* (Fig. 2).

Antifungal resistance: 19.14% of fungi grown in retropositive patients were resistant to Fluconazole but sensitive to

Amphotericin B, compared to 14.28% in retronegative patients. 4.25% of the fungi grown in retropositive patients were resistant to both Fluconazole and Amphotericin B but were sensitive to Caspofungin. None of the fungi grown in retronegative patients were resistant to Amphotericin B.

Discussion

A total of 500 samples each were taken from upper back, web spaces of toes, inguinal region, dorsum of tongue in HIV positive and HIV negative individuals. Both KOH and culture positive were seen in 3.6% of all the samples in the HIV positives and 1.6% in the HIV negatives *p*-value was <0.001, odds ratio 37.41 C.I., for odds ratio 15.22–91.97. Therefore, in HIV positive individuals KOH and culture positivity was significantly more than HIV negatives. Among all the areas investigated, dorsum of tongue showed the highest percentage of incidence. Second in frequency of involvement in the HIV positives were the web spaces of toes, groin and subungual scrapings at 6% each followed by interscapular region at 4% were seen. A case-control study in 102 renal transplant recipients the prevalence of superficial mycoses was 63.7% as compared to 30.7% in the control.⁵ A similar study done on cancer patients on immunosuppressive therapy revealed that 79% of apparently normal skin in the toe webs were KOH and culture positive.⁶ In the present study, 57% of HIV patients had at least one fungal infection whereas 21% of HIV negative patients had at least one fungal infection. This finding was similar to that of Petmy et al.¹ study, where the prevalence of superficial fungal infections in HIV positive patients was 53%. The most common fungal infection in HIV positive individuals was mucocutaneous candidiasis, seen in 36% of HIV positive individuals who participated in this study. In a study by Jindal et al.,¹⁴ mucocutaneous candidiasis was seen in 26.5% of HIV seropositive patients. Another study by Kumarasamy et al.¹⁵ observed that oral candidiasis affected 45% of HIV positive patients. In contrast, Petmy et al.¹ and Baradkar¹⁶ reported a higher prevalence of oral candidiasis in HIV positive individuals, i.e. 77% and 63.93% respectively.

In our study, the most common species of mucocutaneous candidiasis noted was *C. albicans* (80.55%). In a study by Vaishali et al.,¹⁷ 66% of candidiasis was caused by *C. albicans*. Various other studies showed different prevalences of *C. albicans*, Lopaz-Dupla et al.,¹⁸ reported 44%, Korting et al. reported 74% and McCreary et al. reported 100% *C. albicans* in their study populations.¹⁹

Dermatophytic infections were seen in 22% of HIV positive patients and in 13% of HIV negative patients in the present

Table 3 – Correlation of types of fungal infections with CD4 count in retropositive patients.

Type of infection	CD4 > 500 cells/μl	CD4 200–499 cells/μl	CD4 < 200 cells/μl	Total
Candida	02	11	21	36
Dermatophyte	07	06	09	22
Non dermatophyte moulds	00	00	02	02
Pityrosporum	02	03	03	08
Others	00	00	01	01

Table 4a – Types of fungal infections in retropositive patients.

Types	No of patients with infection	% of fungal infection (n = 57)	% of patients (n = 100)
Candida	36	63%	36%
Dermatophyte	22	38%	22%
Non dermatophyte moulds	02	3.5%	2%
Pityrosporum	08	14.03%	8%
Others (Mucor-Cunninghamella)	01	1.75%	1%

Table 4b – Types of fungal infections in retronegative patients.

Types	No of patients with infection	% of fungal infection (n = 21)	% of patients (n = 100)
Candida	02	9.5%	2%
Dermatophyte	13	61.9%	13%
Non dermatophyte moulds	01	3.03%	1%
Pityrosporum	06	28.57%	6%
Others	02	09.5%	2%

Fig. 2 – (a) Extensive Tinea corporis. (b) Tinea cruris. (c) Thin walled smooth multiseptate macroconidia and grape like clustered microconidia along the hyphae on Lacto phenol cotton blue mount suggestive of *Trichophyton mentagrophytes*. (d) *Trichophyton rubrum* colonies on Sabouraud's agar showing white downy to pink granular colonies. (e) Hyphae with teardrop microconidia along the sides and smooth walled pencil shaped macroconidia on Lacto phenol cotton blue suggestive of *T. rubrum*.

Fig. 3 – (a) Nodular lesions on back in a retronegative patient caused by *P. variotti*. (b) Deep mycoses in hand of a retronegative individual caused by *Rhizopus microspores*. (c) Subcutaneous abscesses in a retropositive individual caused by *Cunninghamella*. (d) Nodules and ulcers in a retropositive individual caused by *Penicillium marneffi*.

study. Much lesser prevalence in HIV positive patients were reported by Rajesh et al.²⁰ as 6.06% and Vaishali et al.¹⁷ as 8%. Jindal et al.¹⁴ reported 13.2% of HIV seropositive patients to be having dermatophytic infections whereas Kaviarasan et al.²¹ observed the prevalence to be 22.2% which is very similar to our study. The commonest dermatophyte grown in both HIV positive and HIV negative patients in this study was *T. rubrum*

(54.54% and 69.23% respectively) followed by *T. mentagrophytes* (27.27% and 30.76%). In a study by Grover et al.,²² in normal individuals the commonest dermatophyte isolated was *T. tonsurans* (20.5%), followed by *T. rubrum* (8.7%). The non-dermatophyte species grown in HIV positive patients were *Nattrasia mangiferae* and *Aspergillus flavus* and the one grown in HIV negative patient was *Aspergillus fumigates*

Fig. 4 – (a) Hairy, dark grey to blackish brown colonies of *Natrassia mangiferae*. (b) Chains of arthroconidia of *Natrassia mangiferae*. (c) *Rhizopus microspores* colonies on sabouraud's agar. (d) Slide culture mount of *Rhizopus microspores*.

(Fig. 4). The prevalence of superficial mycoses in non HIV patients in an Indian study showed dermatophytosis in 70.5%, candidiasis in 20.5% and *P versicolor* in 9.0%.²³ In another study in AIDS patients the prevalence of dermatophytoses was 48.5%, pityriasis versicolor 23.6% and candidiasis in 17.1%.²⁴ Studies have been few and their results were varying. This study showed many atypical fungi causing cutaneous infections in both HIV positive and HIV negative patients. Two HIV negative patients had uncommon fungal infections in the form of *Paecilomyces variotti* (Fig. 3a), and *Rhizopus microspores* (Fig. 3b). *Cunninghamella*, a type of *Mucor* was grown from multiple abscesses (Fig. 3c) and cutaneous nodules and ulcerative plaques caused by *Penicillium marneffi* (Fig. 3d) were seen in HIV positive patients. More than 75% of the fungi cultured were sensitive to Fluconazole, the figures being 76.59% in HIV positive and 85.71% in HIV negative patients. The rest were found to be sensitive to Amphotericin B except

4.25% fungi in HIV positive patients which were found to be sensitive to Caspofungin only.

Conclusions

The findings of this study suggest that the apparently normal skin of HIV/AIDS patients harbour fungi more frequently than HIV negatives even in the absence of visible clinical signs. This increased frequency of colonization by fungal species, compounded with the immunocompromised status of the host may be the cause for the higher incidence of fungal infections among HIV positive patients observed in the present study. Moreover, uncommon species of fungi were involved in HIV positive individuals when compared to the general population. It was also evident that the species isolated from the HIV positive patients had a higher incidence of resistance to the

commonly used antifungal medications. This may pose challenges in effectively managing such infections in immunocompromised individuals in the era of increasing fungal resistance, and measures to prevent such patients from getting exposed to various fungal species may prevent the possibility of colonization and thus reduce the incidence of them developing fungal infections.

Recommendations

In view of the findings in this study the following recommendations to prevent nosocomial infections, are suggested for HIV/AIDS wards to minimize the risk of acquiring fungal infections (a) Placement of wards should be away from other infectious disease wards/acute wards. Sites such as soil contaminated with bird, pigeon or bat droppings, older urban and rural structures and decaying vegetation/trees should be avoided when establishing these wards as they carry fungal spores.²⁵ (b) Other hospital environmental measures include air conditioning, hospital rooms supplied with sterile laminar airflow (LAF); and installation of high efficiency particulate air (HEPA) filters. (c) Antifungal-resistant fungi should be kept in mind while treating fungal infections and fungal culture, antifungal testing should be part of the evaluation in all AIDS patients. This facility should be made available at all immune deficiency centres.

Conflicts of interest

The authors have none to declare.

Acknowledgements

This paper is based on Armed Forces Medical Research Committee Project No. 4122/2011, granted by the office of the Directorate General Armed Forces Medical Services and Defence Research Development Organization, Government of India.

Nb Sub Rao, Department of Microbiology, Armed Forces Medical College, Pune for fungal culture, staining, species identification and anti fungal sensitivity test.

REFERENCES

- Petmy LJ, Lando AJ, Kaptue L, Tchinda V, Folefack M. Superficial mycoses and HIV infection In Yaounde. *J Eur Acad Dermatol Venereol*. 2004;8:301–304.
- Kar KH, Narayan R, Gautam RK. Mucocutaneous disorders in HIV Patients. *IJDVL*. 1996;62:283–285.
- Thappa DM, Kaviarasan PK. Spectrum of cutaneous disorders in HIV patients. A hospital based study. *JIMSA*. 2004;17:226–228.
- Spira R, Mignard M, Doutre MS. Prevalence of cutaneous disorders in a population of HIV infected patients in South Western France 1996. *Arch Dermatol*. 1998;134:1208–1212.
- Tülin A, Müge G, Demirbilek, et al. Superficial fungal infections in 102 renal transplant recipients: a case-control study. *J Am Acad Dermatol*. 2003;49(2):187–192.
- Alteras GA, Feuerman EJ. The prevalence of pathogenic and potentially pathogenic fungi on the apparently healthy skin of patients with neoplastic diseases. *Mycopathologia*. 1980;71:85–87.
- Ashman RB, Farah CS, Wanasaengsakul S, et al. Innate versus adaptive immunity in *Candida albicans* infection. *Immunol Cell Biol*. 2004;82:196–204.
- Diz Dios P, Ocampo A, Otero I, Iglesias I, Martinez C. Changes in oropharyngeal colonization and infection by *Candida albicans* in human immunodeficiency virus infected patients. *J Infect Dis*. 2001;183:355–356.
- Jones HE, Reinhardt JH, Rinaldi NG. Acquired immunity to dermatophytosis. *Arch Dermatol*. 1974;109:840–848.
- Rush FM, Black H, Dingly JM. Onychomycosis caused by *Fusarium oxysporum*. *Aust J Dermatol*. 1971;12:18–29.
- Anaissie EH, Kantarjian P, Jones B, et al. A newly recognized fungal pathogen in immunosuppressed patients. *Cancer*. 1986;57:2141–2145.
- Grossman ME, Fithian EC, Behrens C, Bissinger J, Fracaro M, Neu HC. Primary cutaneous aspergillosis in six leukemic children. *J Am Acad Dermatol*. 1985;12:313–318.
- Thappa DM. Mucocutaneous fungal infections of significance in HIV infected individuals of India. *Ind J Dermatol*. 2001;46:203–211.
- Jindal N, Aggarwal A, Kaur S. HIV seroprevalence and HIV associated dermatoses among patients presenting with skin and mucocutaneous disorders. *Indian J Dermatol Venereol Leprol*. 2009;75:283–286.
- Kumarasamy N, Solomon S, Mahivanan P. Dermatologic manifestations among HIV virus patients in South India. *Int J Dermatol*. 2000;39:192–195.
- Baradkar. Isolation and characterization of *Candida* species in AIDS. *IJMM*. 1998;17(1):42–45.
- Vaishali W, Anju K, Renu B. Characterization of *Candida* species from oral thrush in Human Immunodeficiency Virus (HIV) seropositive and seronegative patients. *Bombay Hosp J*. 2008;50(2).
- Lopaz-Dupla M, Sarz PM, Garcia VP, Ortega EV, Uriol PL. Clinical, endoscopic immunologic and therapeutic aspects of oropharyngeal and esophageal candidiasis in HIV infected patients: a survey of 114 cases. *Am J Gastroenterol*. 1992;87(12):1771–1775.
- McCreary C, Bergin C, Pilkington R, Kelly G, Mulcahy F. Clinical parameters associated with recalcitrant oral candidosis in HIV infection: a preliminary study. *Int J STD AIDS*. 1995;6:204–207.
- Rajesh R, Subramanyam K, Padmavathy BK. Prevalence and species profile of dermatophytes among HIV positive patients in rural Referral Centre. *Ind J Sex Transm Dis*. 2006;27(2):70–74.
- Kaviarasan PK, Jaishankar TJ, Thappa DM. Clinical variations in dermatophytes in HIV infected patients. *IJDVL*. 2002;68:213–216.
- Grover S, Roy P. Clinico-mycological profile of superficial mycosis in a Hospital in North-East India. *MJAFI*. 2003;59:114–116.
- Kannan P, Janaki C, Selvi GS. Prevalence of dermatophytes and other fungal agents isolated from clinical samples. *Indian J Med Microbiol*. 2006;24(3):212–215.
- Goodmon DS, Telplitz ED, Wilshner A, et al. Prevalence of cutaneous disease in patients with acquired immunodeficiency syndrome (AIDS) or AIDS-related complex. *J Am Acad Dermatol*. 1987;17:210–220.
- Fungal meningitis. *Centers for Disease Control and Prevention, National Center for Immunization and Respiratory Diseases*. U.S. Department of Health & Human Services, HHS/Open, USA. gov; 2016, April.