

FUNGAL INFECTIONS IN HIV INFECTED CHILDREN

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Abstract

HIV as we all know remains to be a global pandemic. HIV infection causes gradual loss of immune system particularly the cell-mediated immunity and hence, predisposing a person to several opportunistic infections including fungal infections. Fungal infections vary in their course depending on geographical regions. Lack of information on patterns of fungal infections initiated us, to conduct this study. Fifty-five HIV sero-positive patients admitted in Civil Hospital, Ratlam, India, during January 2008 to January 2009 were included in this study. The study group comprised of 32 (58.18%) males and 23 (41.81%) female patients. Relevant clinical samples were processed for detection of fungal pathogens using standard mycological technique. Fungal infections were suspected in 43 (78.18%) of the patients. *Candida* species topped the list being present in 27 (62.79%) of the patients, mostly in the form of oropharyngeal Candidiasis. Two patients presented with systemic Candidiasis. Cryptococcal meningitis and Dermatophytosis was documented in equal proportions being in 6 (13.95%) each. *Geotrichosis candidum* in 4 (9.30%) patients were other fungal infection encountered. *Pneumocystis carinii* (*Pneumocystis jiroveci*) in spite of being suspected clinically in 11 (20%) patients could not be confirmed microbiologically.

Keywords- HIV, Fungal infections, Candidiasis, children

Introduction

Infection with HIV results in progressive loss of host immune mechanism. Compromised immune status predisposes to a wide variety of opportunistic infections, being the major cause of morbidity and mortality in these patients [1,2]. However, these patients are subjected to a wide spectrum of pathogens, fungal infections play an important role. As these infections differ in different geographical boundaries, knowledge about the spectrum of them is crucial for clinicians [1, 3]. The number of HIV and AIDS cases is gradually increasing with a lack of knowledge about the disease in general population in this region of India. This study was planned to know the pattern of fungal infections in HIV sero-positive patients with various clinical presentations.

Material and Methods

A total of 55 HIV seropositive patients admitted in Civil Hospital, Ratlam, India, during January 2008 to

January 2009, were included in the study. HIV infection in these patients was confirmed by at least two different ELISA kits as per WHO strategy II. Whenever needed Western blot (Qualicode Transasia India) was used for confirmation. Detailed clinical history and physical examination was done.

Depending upon clinical presentation, various clinical samples were collected i.e. sputum, urine, blood, CSF, pleural fluid, ascitic fluid, oral scraping, broncho-alveolar lavage, induced sputum, skin scraping, etc. in sterile container and sent to the microbiology laboratory. Samples were processed as per standard mycological technique 4. Each specimen was examined for the presence of fungus by microscopy using wet mounts (KOH mount, Nigrosin) or stained preparations (Gram stain Giemsa stain, or Gomoris methenamine silver stain). Isolation of the fungus was done using Sabouraud dextrose agar (SDA) with antibiotics and with or without cycloheximide and sunflower seed agar [5]. The plates were incubated in two sets, one at room temperature and another at 35° Celsius for a minimum of four weeks. Growth rate, colony characteristics, and microscopic morphology were used to identify the isolate. *Candida* was identified to species level by germ tube test, growth morphology on cornmeal agar and pattern of sugar assimilation.

Serum and CSF samples from suspected cryptococcal infection were subjected to enzyme immunoassay by premier cryptococcal antigen detection kit. Forty HIV positive serum samples were also subjected to fungal immune-diffusion system for detection of precipitating antibody to *Histoplasma capsulatum*. Forty HIV seronegative samples were randomly selected and run simultaneously as negative control.

Results

Out of 55 patients examined, 32 were males 23 females (age group 5-22 years). Though in majority of the patients mode of transmission could not be elicited (24/55), vertical transmission still remains the major mode of transmission (13/55) followed by blood transfusions and drug abuse (11/83), and only (7/55) had acquired HIV through sexual transmission (Table-1). Most of these patients came either from low socioeconomic status; farmers or from low wage earners. All the patients were positive for HIV-1; one patient was co-infected with HIV-2. Five patients were co-infected with hepatitis B virus.

All patients presented with more than one symptom, persistent cough (46/55) and fever (41/55) being the most common followed by weight loss more than 10% of body weight in last three months (29/55), chronic diarrhea (15/55), generalized lymphadenopathy (10/55) and altered sensorium (6/83) (Table-2).

Fungal infections were suspected in 49/55 patients but confirmed microbiologically in 43 (78.18%) cases as shown in (Table 3). Candidiasis either in the form of oropharyngeal, esophageal, urinary or systemic topped the list 27 (62.79%) followed by Cryptococcal meningitis 6 (13.95%) and Dermatophytosis 6 (13.95%). Among these 27 samples of Candida infection, C.albicans was the main species found in 19 (70.37%) followed by C. nonalbicans in 8 (29.62%). This included two C. kefyr and C. parapsilosis

each and one C. krusei. Geotricum candidum was found in 4 (09.30%) cases, as co-infection with C albicans. Urinary tract infection (UTI) due to fungus was found in six cases. Candida albicans was the main organism causing UTI found in three cases followed by two Geotricum candidum one C. kefyr. Candida species isolated from sputum samples was regarded as oral contamination as most of the patients had oral Candidiasis. Cryptococcal antigen in CSF, was detected in 6 (13.95%) out of eleven clinically suspected cases of cryptococcal meningitis. [Table-4]

Six patients had widespread Dermatophytosis caused by Trichophyton rubrum in four cases and Microsporum gypseum in two. Histoplasma capsulatum antibodies could not be detected in any of the test or control serum samples.

Table -1 Routes of HIV transmission (n=55)

Routes of transmission	No (%)
Vertical transmission	13 (23.63%)
Blood transfusion + drug addicts	11 (20.00%)
Sexual route	07 (12.72%)
Unknown	24 (43.63%)

Table – 2 Clinical spectrum of patients with HIV infection (n=55)

Symptoms	Numbers (%)
Chronic cough	46 (83.63%)
Persistent fever	41 (74.54%)
Weight loss	29 (52.72%)
Chronic diarrhea	15 (27.27%)
Generalized lymphadenopathy	10 (18.18%)
Altered sensorium	06 (10.90%)

Table -3 Sample wise distribution of fungal isolates (n=43)

Type of specimen (no)	Fungal isolates found to be positive (no)	Type of isolates (no)
Oral scrapings (42)	23	C. albicans (14) C. nonalbicans (7) G. candidum (2)
Urine (28)	06	C. albicans (3) C. nonalbicans (1) G. candidum (2)
Blood (22)	02	C. albicans (2)
CSF (11)	06	C. neoformans (6)
Skin scrapings (9)	06	T. rubrum (4), M. gypseum (2)
Sputum (23)	00	-
Total (135)	43	

Table -4 Spectrum of fungal infections in HIV/AIDS patients (n=55)

Type of fungus	Clinically suspected in	Confirmed microbiologically
Candida species	30	27
G. candidum	5	4*
P. carinii	11	-
Cryptococcus species	11	6
Dermatophytosis	6	6
Histoplasma species	-	-
Aspergillus	-	-
Total	49 (89.09%)	48 (78.18%)

*Co-infection

Discussions

HIV is a deadly disease having its impact on different age groups but specially affecting the productive age people. Implementation of methods to prevent HIV through vertical transmission remains to be a major challenge in the study zone. The age and sex distribution in this area of Madhya Pradesh has not changed over the last ten years [7]. Male to female ratio in this study was found to be 1:3 similar to a study done in Pondicherry, India, where male to female ratio was 1:6 showing a male predominance [6]. In majority of patients no history of sexual contact or BT was elicited probably showing an awareness about the sexual mode of transmission and possibly a non revealing fact on the part of patients. Parents HIV status was unknown in many cases.

Candidiasis in the form of oral/ esophageal/ pharyngeal involvement is the most common fungal infection affecting HIV seropositive patients, contributing significantly to their mortality and morbidity [2, 8]. Ninety percent of patients develop some form of Candida infection at some time of the disease [2, 8]. *C. albicans* is the most common species but other species like *C. tropicalis*, *C. krusei*, *C. glabrata* are also involved [9]. We found 23 (53.488%) patients suffering from oral Candidiasis. Out of which, 10 gave a history of dysphagia suggesting possible esophageal involvement. This has shown the increasing significance of *C. nonalbicans* in HIV infected patients. Species identification of Candida becomes more important keeping in mind the inherent resistance of some Candida spp. to some antifungal agents. Other studies have found the incidence of Candidiasis ranging from 30-70% [1,3]. Candida infections in AIDS cases are usually limited to superficial mucosal involvement. Candidemia occurs rarely [8]. We had only two cases with systemic involvement.

The second common fungal pathogen that was suspected (on the basis of specific presentation like interstitial pneumonia, excessive dyspnea with PO₂ imbalance etc) in these patients was *Pneumocystis carinii* now called as *Pneumocystis jiroveci* as a cause of *Pneumocystis pneumonia* (PCP). PCP is more commonly reported from Western World [10]. In the USA 60-70% of AIDS cases had PCP as their presenting illness with a mortality of 10-20% [10,11]. The reported incidence of PCP

in Indian patients is 4% [3]. We had 11 patients with strong clinical suspicion of PCP but could not be confirmed microbiologically either due to lack of expertise in technique or inappropriate sample collection or possibly due to common

practice to start PCP prophylaxis. Information on the incidence of PCP in Indian patients is very limited [3, 10, 11].

Cryptococcal meningitis is a common life threatening infection in AIDS patients [3, 12-15]. The incidence in HIV infected patients is highly variable ranging from 6-10% in the USA, West Europe, Australia, and France to 15-30% in sub-Saharan countries [12, 13]. Cryptococcal infection was reported for the first time in India in 1952, and since then there are many reports of Cryptococcal infection particularly meningitis in HIV infected individuals [12, 15]. Indian studies have shown variable incidence ranging from 5.6% in Lucknow, India to 34.8% in Tamilnadu, India [15]. We found six patients means 13.95% incidence of Cryptococcal meningitis with 50% mortality. Other fungal pathogens which have been found in HIV infected individuals included histoplasmosis, coccidioidomycosis, penicilliosis and aspergillosis. None of these infections could be detected in our study. Aspergillosis is not as common in AIDS cases as is found in patients with neutropenia and steroid therapy [3]. There are sporadic reports of histoplasmosis in Indian patients [16, 17] particularly with oral involvement but we found histoplasmosis in none of our patients.

Dermatophytes have not been mentioned as important pathogens in HIV infected individuals but it is known that these patients have atypical presentation with more extensive involvement [2]. This was evident in our study as we had six patients out of which four had extensive involvement due to *Trichophyton rubrum* and two had *Microsporum gypseum*. In conclusion it appears that Candida and Cryptococcus are the main fungal pathogens in this part of the country as well as in other parts of India. The incidence and species are variable depending upon geographical area. More efforts are needed to give laboratory evidence of *Pneumocystis pneumonia*. Knowledge about the pattern of pathogens is a must in order to serve the HIV infected patients better.

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