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Asymptomatic candiduria in HIV seropositives attending an ART centre in a tertiary care hospital

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ABSTRACT

BACKGROUND

Most of patients with candiduria are asymptomatic. However, in immunocompromised patients like HIV-infected individuals, it has high risk of morbidity and mortality as it is a good indicator of disseminated infection and fungemia.

AIM

To isolate and characterize Candida species in HIV seropositives patients with asymptomatic candiduria and to determine distribution of Candida species in different CD4+ cell counts categories.

MATERIALS AND METHODS

The study group comprised of 55 males and 45 females, of which 50 were on ART and 50 were not on ART. Clean catch mid stream urine specimens were collected from patients and urine was inoculated on SDA, incubated at 37⁰ for 48-72 hours.

RESULTS

14 of 100 subjects had candiduria. Out of 14 Candida species, 5 candida albicans and 9 non-albicans candida species were isolated. The prevalence of candiduria was high among patients who were not on HAART (43%) than in individuals who were on HAART (18%) with CD4+ count >200 cells/ μ l.

CONCLUSION

Measures to reduce candiduria prevalence, such as early diagnosis, prompt treatment with appropriate antifungals and strict compliance with HAART regimen are advocated to reduce the morbidity and mortality in HIV positive patients.

Keywords: CD4+cell count, HAART, SDA, Urine.

INTRODUCTION

The human immunodeficiency virus (HIV) has emerged as a global disaster(1) HIV/AIDS continues to spread globally and remains a worldwide pandemic affecting about 40 million people².(2)

AIDS is caused by HIV and is characterized by progressive damage to the immune system, which opens the door to different opportunistic infections including fungal infections.(3)

The commonly encountered fungal infections in HIV-positive patients are candidiasis, cryptococcosis, histoplasmosis, pneumocystosis, coccidioidomycosis, and penicilliosis.(4)

These infections said to be opportunistic are responsible for increase morbidity within 5 to 10 yrs. Candidiasis affects more than 80% of HIV infected subjects.(3) Candida species are ubiquitous fungi and are the most common fungal pathogens that affect humans. The growing problem of mucosal and systemic candidiasis reflects the enormous increase in the pool of patients at risk and the increased opportunity that exists for Candida species to invade tissues normally resistant to invasion.(5)

Candida is the fourth principle cause of urinary tract infection (UTI) in HIV infected patients after E.coli, Pseudomonas aeruginosa and Enterococci. Candiduria is typically asymptomatic and may be thought of as a somewhat benign infection; nevertheless it can significantly increase the costs of hospitalization, relative to other urinary tract infections.(2) Candiduria is not usually looked for in general practice yet, it can be the source of disseminated infection in immunocompromised individuals.(3)

C. albicans has been the yeast most commonly isolated from urine, accounting for 50%–70% of isolates in various studies. C. glabrata and Candida tropicalis are the next most common species found in cultures of urine. C. parapsilosis is found more often in urine from neonates and is usually associated with systemic infection in this population. However, many hospital laboratories do not speciate yeasts that are isolated from urine unless specifically requested to do so. Thus, changes or trends in species causing candiduria cannot easily be tracked.(6)

The pathogenesis of candidal infection is extremely complex and probably varies with each species. Adhesion of candida organism to the epithelium of the gastrointestinal or urinary tract is a crucial factor.(7)

Fungal infections caused by the yeast pathogens remain quite common in immunocompromised host, especially in HIV infected individuals. Infections with Candida appear when the CD4 count is 200-500 cells/ μ l and may be the first indication of immunodeficiency. These infections are playing an increasing important role in the morbidity and mortality of HIV/AIDS patients. Although the use of highly active antiretroviral therapy (HAART) has

decreased the incidence of fungal infections, candidiasis continues to afflict HIV infected individuals in HAART era. Unfortunately, prolonged use of antifungal among this population has led to increased incidence of resistance.(8)

Since the advent of HAART, the incidence of specific fungal and parasitic opportunistic infections in human immunodeficiency virus disease has been decreased.

Asymptomatic candiduria is usually benign in most patients and do not require antifungal medication. However, in immunocompromised patients, it has a high risk of morbidity and mortality.(4)(9)

Decreased CD4+ cell counts in HIV/AIDS patients predispose them to Candida infections. This study was carried out to determine distribution of Candida species in different CD4+ cell counts categories and compare the prevalence of Candida spp.in HIV infected patients on antiretroviral therapy with that not on antiretroviral therapy.

MATERIALS AND METHODS

This prospective study was carried out at Mysore medical college and research institute in Mysore from Jan 2013 to July 2013. One hundred HIV seropositive subjects who were attending Anti retroviral treatment centre, as out patients without any urinary symptoms were included in the study. Patients with diabetes mellitus and with urinary symptoms were excluded from the study. Informed consent was obtained & enrolled after due counselling from all subjects prior to specimen collection.

The study group comprised of 55 males and 45 females, of which 50 were on ART and 50 were not on ART. The parameters like biodata, history of use of antibiotics and antifungal therapy were noted.

Clean catch mid stream urine specimens were collected from participants using wide mouth transparent sterile screw capped container. Participants were instructed on how to collect mid-stream urine samples. A loopful of centrifuged urine sediment was transferred onto a glass slide for direct wet mount preparation for the presence of yeast-like cells and inflammatory cells. The presence of typical colonial oval or ellipsoidal yeast-like morphology was used as an indicator for the presence of yeast and branching pseudohyphae characteristically typical of

Candida. Smears were made and Gram stained and latter observed at 100X for fungi elements.

For culture, a loopful of the urine (using a 0.01 ml of an inoculating wire loop) was inoculated onto Sabourauds Dextrose Agar (SDA) plate supplemented with chloramphenicol using the streak-out plate method. Inoculated SDA plates were incubated aerobically at 37°C for 48-72 hours. The plates were examined for the presence of growth after 48 h of incubation. Colonies that were raised had white to cream coloured, smooth, glabrous like appearance and those with distinct yeast-like odour were preliminarily tagged as Candida species. Urine specimens with Candida colonies more than 10⁵ CFU/ml were considered as significant.

Colonies were further identified by Gram stain and purified by a repeated streaking method on the same medium to obtain pure discrete colonies. These were subsequently grown and maintained on an SDA slant

at 4°C and were stored for species identification. The speciation was done on the basis of germ tube formation and corn meal morphology.

The CD4+ T cells count was determined from study participants using FACS CALIBER and the counts were categorised according to standards of the WHO, as severe when counts <200 cells/μl; low (200–349cells/μl); moderate (350 – 499cells/μl).

RESULTS

Out of 100 participants, 14 had asymptomatic candiduria. Females accounted for the higher prevalence 59(64%) compared to 9(36%) in males. The participants were between 20 to 70 years of age (mean age of 33 years). Among 14 asymptomatic candiduria participants, 10 were on HAART and 4 were not on HAART. The CD4+ count was ranging from 50 to 700 cells/μl.

Table 1: Prevalence of candiduria in different CD+ cell count categories

	Status/CD4 count Cells/μl	No of samples	No of participants with Candiduria
Not on ART	<200	07	3(43%)
	≥200 to 349	08	1(12.5%)
	≥350	35	2(6)
On ART	<200	32	6(18%)
	≥200 to 349	08	1(12.5%)
	≥350	10	1(10%)

Characteristic of Candia species

Of the 14 Candida species isolated, 5(36%) were germ tube positive and identified as Candida albicans and further confirmed by corn meal morphology.

Remaining 9 non-albicans species identified were: Candida tropicalis 3 (21.5%), Candida glabrata 3(21.5%), Candida guilliermondi 2 (14.50%) and Candida kefyr 1 (7.25%).

Table 2: Distribution of Candida species among participants on HAART and not on HAART

Species	Nos	On HAART	Not on HAART
Candida albicans	05	3	2
Candida tropicalis	03	2	1
Candida glabrata	03	1	2
Candida guilliermondi	02	1	1
Candida kefyr	01	1	0
Total	14	8	6

DISCUSSION

The risk of fungal infection depends primarily on these factors: the severity of impairment of cell-mediated immunity; the risk of exposure; recent or current use of an antifungal medication; and neutropenia that relates primarily to invasive candidiasis(4)

HAART has generally been taken as the gold standard in the management of HIV patients. The use of HAART results in improved quality of life for HIV patients as well as near normal turnover of both CD4 and CD8 T-cell populations. Therefore, it is expected that in the era of HAART, immunity of HIV patients will be improved and opportunistic infections reduced.(4)

The prevalence of asymptomatic candiduria in the present study is 14%. This result is in line with studies of Esebelahie et al(8) showed prevalence of 13.5% and Longdoh A. Njunda et al (10) showed 12.5%. Even in the HAART era, the rate of isolation of candida is increasing which might be due to the late initiation of ART.

In this study candiduria was observed more frequently in females (76.80%) than in male (23.20%). The higher incidence found may be connected to the general increased risk of women to acquiring UTI. This is due to the anatomical structure of the female genital tract that makes them susceptible to UTI compared to males irrespective of their HIV sero status.

The prevalence of candiduria in this study was higher among patients who were not on HAART (43%) than in individuals who were on HAART (18%) with CD4+ count < 200 cells/ μ l. This finding is supported by earlier observations of Esebelahie N.O.et al.(8) and Longdoh A.Njunda et al.(10) It has been reported that fungal agents such as Candida takes advantage of immune suppression seen HIV patients as a result CD4+ T cells depletion. It has also been reported that number of experimental studies that resistant to Candida infection is dependent upon the participation of T-lymphocytes.

Among Candida isolates in this study, Candida albicans (36%) was the predominant isolate and other non-albicans species are Candida tropicalis (21%), Candida glabrata (21%), Candida guilliermondi (14.50%), Candida kefyr1 (7.25%). These results are comparable with studies Longdoh A.Njunda et al.(10) J.P.Lohoue et al (3) and Wadhwa et al.(11) In most studies C. albicans dominates and accounts for 50% to 70% of all Candida-related urinary isolates, followed by C. glabrata, and C. tropicalis. The possible reasons why Candida albicans constituted a large majority of the Candida species could possibly be due to its wide distribution in nature and its possession of multiple adhesins which gives this pathogen the ability to readily colonise host environment by adhering to host mucocutaneous cells.

It has been reported that candida infections among HIV patients are refractory to antifungal agents, thus making this infection life-threatening among HIV patients.(6)

CONCLUSION

Candidiasis remains an important opportunistic infection among HIV patients. Although C. albicans remains the main responsible species, non-C.albicans species are also emerging as pathogens.

Asymptomatic candiduria is more in the patients with lower CD4 count which warrants the early initiation of HAART and could be useful for candida spp.infections by using antifungal drugs when CD+ T count falls under 200 cells/ μ l.

Candiduria although benign may be an indicator of an advanced stage of AIDS. We would recommend routine urinary investigation for candiduria in the management of patients living with HIV. Measures to reduce its prevalence, such as early diagnosis, prompt treatment with appropriate antifungals and strict compliance with HAART regimen, are advocated to reduce the morbidity and mortality.

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