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STUDY OF CHRONIC DIARRHOEA IN HIV POSITIVE PATIENTS WITH REFERENCE TO *CANDIDA ALBICANS*.

Microbiology

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ABSTRACT

Introduction: Bacteria, parasites and viruses are the most important enteropathogens in HIV infected patients. Candida is considered to be the only etiological agent necessary for diarrhoeic symptoms13. Against this context the present study was carried out to identify candida as cause of chronic diarrhoea in HIV positive patients and their association with CD4 T cell count & ART.

Material and methods: A total 208 stool samples were collected and examined for diarrhoeagenic pathogens by using standard microbiological methods. HIV testing was carried out as per NACO guidelines and CD4 T-cell counts were estimated by FACS count system.

Results: Candida albicans was considered to be cause of chronic diarrhoea in 6.25% patients in which no other enteric pathogens were detected and they represent more than 50% of organisms per microscopic field. All Candida albicans were found in the subjects who had CD4 T cell count < 200 cells/µl and significantly more in subjects not taking ART.

Conclusion: Despite reports suggesting a role for Candida species in cases of diarrhoea much of the evidence still remains dubious. This rises the need for additional systematic investigation on the contribution of this genus on infectious diarrhoea etiology among the HIV positive group.

KEYWORDS

Candida, HIV, Chronic diarrhoea

INTRODUCTION:

HIV infected patients are prone to advance a prospect of diseases during their life time.[1] Clinical course of HIV infection is characterized by a decrease in numerals of CD4 T cells and persistent viral replication, resulting in immunological decline.[2] Such progressive decline in immunological responses makes them extremely susceptible to variety of conjoint and opportunistic infections.[3]

Among these opportunistic infections, gastrointestinal tract (GIT) infections are very common in patients with HIV infection or AIDS.[4]

Chronic diarrhoea is a common GIT hurdle in patients with HIV, especially those with forward-looking disease.[5] It significantly diminishes the feature of life in patients with HIV infection and is an independent marker of poor prognosis and also an independent predictor of mortality in patients with AIDS.[7,8]

The etiological spectrum of enteric pathogens causing diarrhoea includes bacteria, parasites, fungi, and viruses[9]. Some studies also demonstrated regional variability of pathogens; as well as changing trends of etiology in same population.[10,11]

Though bacteria, parasites and viruses are the most important enteropathogens which cause infectious diarrhoea in HIV patients, the importance of *Candida* spp. as a colonizer of the gastrointestinal tract of HIV-positive patients is unquestionable.[13] In fact, *Candida* spp. have been reported as opportunistic pathogen of the GIT. They are considered in some situations the only etiological agent necessary for diarrhoeic symptoms.[13] This fungus can take advantage of depressed immune system to become pathogenic. Under these conditions *C. albicans* could grow and cause diarrhoea.[14] The emergence of pandemic of AIDS has changed total scenario of opportunistic fungal infections which can cause considerable morbidity and mortality. Infections with *Candida* spp. have been recognized as important complication of HIV infection since early years of AIDS epidemic.[15]

Appropriate management of OI's is as important as Anti-retroviral therapy (ART) in preventing mortality and morbidity among HIV-infected persons**.** In the west, the incidence of OI's has markedly declined because of the widespread availability of highly active antiretroviral therapy (HAART).[16]

Knowledge of the pattern of the infection can often guide the therapy when resource limitations hamper the exact diagnosis of etiological agent in HIV-associated diarrhoea.[1]

Since diarrhoeal illness due to infective etiology is increasing among HIV infected subjects, clinical microbiologist ought to be aware of wide spectrum of these intestinal infections. Only a few studies regarding candidal diarrhoea and their association with CD4 T cell count are available from our region. Against this background the present study was carried out to identify candida as cause of chronic diarrhoea in HIV positive patients and their association with CD4 T cell count & ART.

MATERIAL AND METHODS:

The study was carried out at Department of Microbiology and ART centre, in a tertiary care hospital. Total 208 HIV seropositive patients with chronic diarrhoea were included in this study. After taking written informed consent, detailed history of each patient was recorded as per the proforma.

Blood and stool specimens were collected from each patient. HIV testing was carried out using commercially available kits as per manufacturer's instruction. CD4 T cell count was performed by automated flow cytometry and the study subjects were categorized in three categories depending on their immune status.

Fresh stool specimens were collected and examined immediately in microbiology laboratory. Macroscopic and microscopic examination of each stool specimen was done. Sabouraud's dextrose agar was inoculated for isolation of Candida. Formal ether sedimentation and Sheather's sucrose floatation methods were used for concentration of stool specimens. Modified Kinyoun's acid fast staining and modified trichrome (Weber) staining were used to rule out opportunistic parasites. Stool specimens were also inoculated on Blood agar, MacConckey agar, Deoxycholate citrate agar, and Lowenstein-Jensen media to rule out bacterial cause of diarrhoea. Identification of bacterial and fungal isolates were carried out using standard microbiological methods.

C. albicans was considered as potential pathogen in HIV positive patients with diarrhoea when no other known enteropathogen was identified and they represent more than 50% of organisms per microscopic field.

RESULTS:

The study population was dominated by males; out of total 208 patients, 136 (65.38%) were males and 72 (34.62%) were females. Male to female ratio was found to be 1.9: 1 in the present study.

Out of a total 208 stool specimens examined in this study, *Candida albicans* was found in 6.25% and other pathogens were detected in 61.53% stool specimens (Table 1).

Table 1. Enteric pathogens detected in the stool specimens (n=208)

Enteric pathogens	No. of stool specimens
Fungi (*C. albicans*)	13 (6.25%)
Parasites	108 (51.92%)
Bacteria	14 (6.73%)
Mixed pathogens	06 (2.88%)
Total	**141 (67.78%)**

Candida albicans was considered to be cause of chronic diarrhoea in 6.25% patients in which no other enteric pathogens were detected and they represent more than 50% of organisms per microscopic field.

The subjects in this study were divided into three groups based on their CD4 T cell counts. Majority of the subjects in this study (68.75%) had CD4 T cell counts below 200 cells/µl while 56 (26.92%) had CD4 T cell counts between 200-499 cells/µl and 9 (4.32%) subjects had CD4 T cell counts above 500 cells/µl as depicted in Table 2.

Table 2. CD4 T cell count of the study population (n=208)

CD4 cell count	No. of subjects
≥ 500 cells/µl	09 (04.33%)
200-499 cells/µl	56 (26.92%)
< 200 cells/µl	143 (68.75%)
Total	**208 (100%)**

All *Candida albicans* were found in the subjects who had CD4 T cell count < 200 cells/µl.

Out of total 208 HIV seropositive patients with chronic diarrhoea, 94 (45.19%) HIV seropositive patients with chronic diarrhoea were taking ART and 114 (54.81%) patients were not taking ART as shown in Table 3.

Table 3. Distribution of study subjects taking ART and not taking ART

Subjects taking ART	Subjects not taking ART	Total
94 (45.19%)	114 (54.81%)	208 (100%)

Out of the total 94 subjects taking ART, *Candida albicans* were isolated in 4 (4.25%) subjects and of the 114 subjects who were not taking ART, *Candida albicans* were isolated in 9 (7.89%) subjects.

DISCUSSION:

In India, the HIV prevalence in males is higher than females.[16] In present study (Table1) also males (65.38%) predominated over females (34.61%). Other studies in India also show male preponderance in HIV infected patients with diarrhoea. Kulkarni et al[4] studied 137 HIV infected patients presented with diarrhoea in which 73% were males and 27% were females. In a study conducted by Uppal et al,[1] 58% were males and 42% were females out of 50 HIV seropositive patients with diarrhoea. In a study by Prasad et al,[6] out of 26 HIV seropositive patients, 77% were males and 23% were females.
Even though bacteria, parasites and viruses being the most important enteropathogens which cause infectious diarrhoea in HIV patients, the importance of *Candida* spp. as a colonizer of the gastrointestinal mucosa of HIV-positive patients is unquestionable.[13] *C. albicans* was isolated in 7.6% to 39.1% stools of patients from different parts of the world. Germani et al[22] in 1998 reported 4.5% *C. albicans* as potential pathogen in HIV positive patients with chronic diarrhoea and Gassama et al[20] in 2001 also reported 7.6% *C. albicans* as potential pathogen in HIV positive patients with diarrhoea when no other known enteropathogen was identified and they represent more than 50% of organisms per microscopic field. Kumar et al[3] in 2002 reported 1.3% *C. albicans* in HIV positive patients with chronic diarrhoea. However, Uppal et al[1] in 2009 reported *C. albicans* in 36% of HIV positive patients with diarrhoea. In Brazil, the results of Rossit et al[18] were comparable with the highest published frequencies (35%) reported in HIV seropositive children.

In our study *C. albicans* was isolated in 13 (6.25%) cases. The stool examination of these patients showed large number (> 50%/ hpf) of yeast cells. No other bacterial or parasitic cause of diarrhoea was detected in these cases.

The etiologic role for an isolated organism in HIV infected patient with clinical symptoms is a major problem. *Candida* spp. is on many occasions the only organism isolated from the intestinal tract of HIV patients with diarrhoea.[17] However, the relevance of candidal infection to the enteropathy and diarrhoea is often associated with HIV is not completely understood. Jaygopal et al[19] in 1992 reported that *Candida* spp. have been implicated in the etiology of chronic diarrhoea and colitis in a patient infected with HIV.

Most of the opportunistic infections are not observed until the CD4 count falls below 200 cells/µl. Association of enteric pathogens with CD4 cell count was assessed. Majority of the subjects (68.75%) had CD4 T cell counts below 200 cells/µl while 26.92% had CD4 T cell counts between 200-499 cells/µl and 4.32% had CD4 > 500 cells/µl. Subjects having *C. albicans* infection had CD4 T cell count < 200 cell/µl.

Appropriate management of opportunistic infections is as important as antiretroviral therapy (ART) in preventing mortality and morbidity among HIV-infected persons.[16] Use of Highly Active Anti-Retroviral Therapy (HAART) as primary therapy of opportunistic infection represent a new model for management which is effective in raising the CD4 count and lowering HIV RNA levels, OIs may completely remit with HAART alone.[12] In the West, the incidence of OIs has markedly declined because of the widespread availability of highly active antiretroviral therapy (HAART).[16] In this study, association of enteric pathogens in subjects taking Anti-Retroviral Therapy (ART) and in those not taking ART was also assessed. Out of the total 208 subjects, 45.19% subjects were on ART and 54.81% subjects were not taking ART.

Candida albicans were isolated in 4.25% (4/94) subjects taking ART and in 7.89% (9/114) not taking ART. *Candida albicans* were detected in high number of patients not taking ART.

Most of the infections in our study were observed in patients who were not taking ART treatment. This elucidate that the patients taking ART are less susceptible to develop an opportunistic infections as it is effective in raising the CD4 count and lowering HIV RNA levels.

Despite reports suggesting a role for *Candida* spp. in cases of diarrhoea much of the evidence still remains debatable. This raises the need for additional systematic investigation on the participation of this genus on infectious diarrhoea etiology among the HIV positive group.

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