

CANDIDURIA IN HIV INFECTED PATIENTS IN YAOUNDE, CAMEROON

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Objective: To detect *Candida* species in the urine of patients living with human immunodeficiency virus (HIV), and correlate the presence of candiduria and CD4 counts.

Patients and Methods: The study population consisted of 105 hospitalized patients from the Military and Central Hospitals of Yaoundé, who either were HIV positive or already suffering from AIDS. The patients consisted of 63 females (60%) and 42 males (40%) giving a male to female ratio of 1:1.5. Midstream urine samples were collected from all patients and mycological examination of the centrifuged sediments was done. Patients with CD4 counts > 499 lymphocytes/mm³ were a proxy control group.

Results: 38 of 105 (36.2%) subjects had candiduria. 71% of the cases were asympto-

matic. The percentage of patients positive versus negative for candiduria increased progressively from stage-A (5%) to B (32%) to C (63%) HIV infection. There was thus a correlation between candiduria and the CDC disease stage. Its presence heralded an advanced immuno-suppressed state of the AIDS patient.

Conclusion: In resource-poor communities, where viral copy and CD4 count determination are expensive, candiduria may serve as one of the indicators for anti-retroviral therapy. We recommend routine detection of candiduria in this high-risk group of HIV/AIDS patients

Key Words: candida infection, CD4 cell count, AIDS, urine

INTRODUCTION

The human immuno-deficiency virus (HIV) is responsible for a complex immune disorder which increases susceptibility to infections. These infections, said to be opportunistic, are responsible for increased morbidity, and a mortality rate estimated at 30-50% within 5-10 years¹. Candidiasis caused by yeasts of the genus *Candida* affect more than 80% of HIV infected subjects^{2,3}. *Candida albicans*, a saprophyte of the human mucosae, is the most frequently isolated species, while other species, saprophytes of the superficial regions, are rarely cultured. *Candida* is the 4th principal cause of urinary tract infection in HIV infected patients, after *Escherichia coli*, *Pseudomonas aeruginosa* and the enterococci^{1,4,5}. Although commonplace, often benign and frequently asymptomatic, candiduria can pose numerous diagnostic and therapeutic problems. The clinical

dilemma with funguria is to distinguish between saprophytism, contamination and infection. The clinical context in this instance is invaluable in making therapeutic decisions.

In Yaoundé, candiduria is not usually looked for in general practice. Yet, it can be the source of disseminated infection in immunocompromised individuals².

PATIENTS AND METHODS

The study population consisted of 105 hospitalised patients from the Military and Central Hospitals of Yaoundé, 63 females (60%) and 42 males (40%) with a male to female ration of 1:1.5. They either were HIV positive or already suffering from AIDS. The most commonly affected age group included the patients between 26 and 35 years of age (43%).

Table 1: Distribution of Candiduria According to CD4 Cell Count

CD4 Count	Positive		Negative		Total	
	No. of Patients	%	No. of Patients	%	No. of Patients	%
<200	18	43%	23	57%	41	59%
200-499	11	42%	15	58%	26	37%
> 499	0	0%	3	100%	3	4%
Total	29	41%	41	59%	70	100%

All patients gave written or verbal consent after the study protocol was explained to them. They were assured that they would receive the same care and consideration, even if they refused to participate in the study. Patients answered questions on a pre-tested and validated questionnaire, assisted by a trained member of the research team (NND), before a complete physical examination was performed. Patients were categorized using the CDC Atlanta HIV/AIDS classification⁶.

After cleaning the urethra and vulvo-urethral regions with antiseptic solution, mid-stream urine was collected in a sterile container and maintained at 4°C during transportation to the laboratory for urine analysis.

Mycological examination of the centrifuged sediments consisted of three steps:

- Microscopic direct examination in a drop of lactophenol-cotton blue.
- Culture on Sabouraud glucose agar to which was added chloramphenicol or chloramphenicol plus cycloheximide at concentrations of 0.5 g/l each. The diagnostic criteria were: presence of at least 30 yeast colonies on direct microscopic examination (LPF) and/or heavy culture of the fungus.
- Identification after 24h incubation at 30°C was done using the Germ tube test, and the physiological characteristics were studied using commercial kits: API 20 C BIO, (MERIEUX SA, 69280 Marcy-L'Etoile, France) and Fungichrome®I (INTERNATIONAL MICROBIO, Parc d'activités-Allée d'Athènes, 83870 Signes, France).

Patients with CD4 counts greater than 499 lymphocytes/mm³ were a proxy control group.

Descriptive statistics (frequencies, means, ratios and tests of variance) were done.

RESULTS

Candiduria was detected in 38 patients (36.2%); 25 females (39.6%) and 13 males (30.9%). The trend of greater disease burden in the female was reflected by the higher ratio of candiduria: 25/63 (39.7%) for females versus 13/42 (30.9%) for males. This difference was not statistically significant due to the small number of patients. Twenty-seven (71%) cases were asymptomatic and 11 (29%) symptomatic.

Of the 38 patients with candiduria, 2 (5%), 12 (32%) and 24 (63%) were of category A, B and C, respectively, according to the Centers for Disease Control (CDC) classification. The degree of infestation with candiduria increased progressively from stage A to C.

The symptomatic patients presented with one or several symptoms and signs: four patients presented with fever, another four with vulval pruritus and three with dysuria, one of the three with severe burning on micturition.

The following risk factors for candiduria were identified: antibiotic use during the month preceding the study in 33 patients, peripheral intravenous catheters in 32, indwelling Foley catheters in two, a nasogastric tube, diabetes mellitus and cancer in one patient each. Twelve patients were under anti-retroviral

therapy; 11 had taken antifungals, and the cancer patient was on antimetabolites.

Of 105 mycological examinations, 38 were positive for fungi but only 33 yeast strains were isolated: *C. albicans* in 29 (76.3%), and *C. tropicalis* in 4 cases (10.5%). Five (13.2%) yeast strains could not be characterized due to reagent and material limitations.

Only 70 of the 105 patients could pay for the CD4 count determination, and the results were as follows: less than 200 lymphocytes/mm³ were found in 41 cases, between 200 and 499 lymphocytes/mm³ in 26, and more than 499 lymphocytes/mm³ in 3 cases (Table 1). The 29 candida-positive results with *C. albicans* were found in the first two groups, i.e. 18 patients (62%) had less than 200 lymphocytes/mm³ and 11 patients (38%) had between 200 and 499 lymphocytes/mm³. The proportions were as follows: 62%, 38% and 0%, respectively, for CD4 count < 200, 200-499 and >499.

DISCUSSION

The hospitals chosen for this study were reference hospitals designated for the diagnosis and management of HIV in Cameroon. The search for *Candida* in the urine of HIV/AIDS patients is not standard practice in these hospitals. Only patients, who gave their written or verbal consent, either directly or indirectly through legal guardians, were included in the study. Patients who hesitated between traditional and modern medical treatment paradigms did not always honor appointments for specimen collection. This in part explains the small study population.

Few studies have been reported on candiduria in Africa, let alone on HIV/AIDS patients. The prevalence of candiduria in our population was 36.2%. This contrasts with the results of other authors. For example, Eholie et al. only reported an incidence of 5.8% of deep fungic infection in their study of profound mycoses in HIV positive or AIDS patients⁷, while Kauffman et al. reported a prevalence of *Candida* of 61.6%⁵. This high disparity in candiduria rates may be explained by the numerous confounding risk factors such as diabetes mellitus, indwelling catheters, intravenous canulas and urinary tract abnormalities being more prevalent in the population of the latter study.

The age and sex distribution in our study reflects the pattern in the general HIV infected population. The affected age groups in our study were patients between 26-35 and 36-45 years of age, which corresponds to the sexually active population. We noted the predominance of females with a sex ratio of 1:1.5 being close to that reported by the UNAIDS/WHO⁸. This prevalence of female HIV patients correlates to a higher prevalence of candiduria in females as well. To attribute candiduria to HIV/AIDS, we would need to carry out a case-control study comparing men and women with and without HIV/AIDS on the one hand and the levels of candiduria on the other. The sample size should be large enough to allow for the control of confounding risk factors for candiduria.

Of the 38 isolates *C. albicans* was the most frequent (76.3%), followed by *C. tropicalis* (10.5%). The predominance of the *albicans* species corroborates reports from Europe published within the last decade^{1,2}.

C. albicans represents half of the etiological agents of candiduria, *C. tropicalis* usually occupies the 3rd place behind *C. glabrata*, which we did not isolate. The identification of 5 yeasts was not possible, either because of technical shortcomings or lack of appropriate reagents. Candiduria was asymptomatic in 71% of our cases; which is close to the percentage reported by Storer et al. (86%)⁹. Fever is a general body response to a variety of ailments. Furthermore, it is a hallmark of HIV infection, whether in the absence or presence of opportunistic infections. It is therefore difficult, even inappropriate, to ascribe fever to candiduria. Fungus balls obstructing the upper urinary tract, which would more than likely cause fever, were not identified in our patients. Minor but irritating symptoms of dysuria, burning and pruritus are known to accompany vulval candidiasis. These were noted in some of our patients. In Kauffman et al's study⁵, urinary symptoms and signs were present in 2-4%. Other conditions associated with candiduria, such as renal lithiasis, genitourinary tuberculosis and urinary malformations¹⁰ were absent in our study.

Serial genotyping, determination of viral load (copies) and CD4 counts are prerequisites for a rational HIV/AIDS treatment program. Thus, patients are started on first-line cheap antiretroviral drugs when CD4 counts dwindle below 200/mm³. Genotyping is essential for the

detection of viral resistance and therefore sensitivity testing to identify reasons for treatment failures. But the costs of such a scheme, however rational, place it out of reach for the resource-challenged countries of sub-Saharan Africa. WHO has, therefore, developed guidelines using, for instance, the complete blood count and patient disease profile to decide on when to treat these HIV/AIDS patients.

It is in this light that we suggest that candiduria may be a cheaper and more accessible marker for patients with CD4 counts less than 200/mm³. We showed that the frequency of candiduria was higher in patients with CD4 counts less than 200/mm³ as opposed to those with counts above 200/mm³. Unfortunately, this difference was not statistically significant, probably due in part to the small sample size, particularly in the group with a CD count above 499/mm³. While awaiting a study with a larger number of samples, and a case-control design, we suggest that candiduria may be a surrogate for CD4 counts in the assessment of HIV/AIDS progression. This may be especially relevant to the cash-strapped populations of sub-Saharan Africa unable to afford CD4 count measurements.

In conclusion, candiduria, although benign, may be an indicator of an advanced stage of AIDS. Therefore, we recommend the integration of routine urinary investigation for candiduria in the management of patients living with the HI-virus.

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RESUME

Candidurie chez les patients infectés par HIV au Yaoundé, Cameroun

Objectifs : Pour détecter des espèces de candida dans l'urine des patients vivant avec HIV, et corrélérer la présence de candidurie au compte des CD4. **Patients et méthodes :** La population d'étude s'est composée de 105 patients hospitalisés dans les hôpitaux militaires et centraux de Yaoundé, tous les patients étaient HIV positif ou souffrant déjà du SIDA. Les patients se sont composés de 63 femmes (60%) et de 42 hommes (40%) avec un sexe ratio de 1/1,5. Des échantillons d'urine du milieu du jet ont été prélevés chez tous les patients et l'examen mycologique des sédiments centrifugés a été fait. Les patients présentant un compte de CD4 de plus de 499 lymphocytes/mm³ étaient un groupe de référence. **Résultats :** 38 des 105 patients (36.2%) ont présenté une candidurie. 71% des patients étaient asymptomatiques. Le pourcentage des patients positifs pour la candidurie a augmenté progressivement du stade A (5%) à B (32%) puis à C (63%) de l'infection par le HIV. Il y avait ainsi une corrélation entre le candiduria et le stade de la maladie de CDC. Sa présence a annoncé un état d'immuno-dépression avancé. **Conclusion :** Dans les communautés de faibles ressources, où la détermination de la répllication virale et du compte de CD4 sont chers, la candidurie peut servir d'un des

indicateurs de la thérapie anti-rétrovirale. Nous recommandons la détection courante de candidurie dans ce groupe de patients à gros risque de HIV/SIDA.

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