Prevalence of serum cryptococcal antigen among HIV infected patients attending a university of Benin Teaching Hospital, Edo state, Nigeria

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Summary

The study was designed to determine the prevalence of serum cryptococcal antigen (CrAg) among HIV-infected patients at the University of Benin Teaching Hospital (UBTH), Edo state, Nigeria. The clinical symptoms, risk factors and past history of some diseases in association with CrAg was determined on 200 HIV-infected patients within the age range of 18 to 71 years, using the cryptococcal antigen lateral flow assay (CrAg LFA). The CD4 count of each patient was determined using the fluorescent-activated cell sorter BD FACS count system. A structured questionnaire was used to gather information on the socio-demographic characteristics, medical and treatment history of patients. Ninety percent of the patients were ART treatment-experi-

enced and 10% were ART naïve. A prevalence of 4.5% cryptococcal antigenemia was observed in the study. The infection rate was higher among the ART naïve patients 5/20 (25%) than in the treatment-experienced group 4/180 (2.2%). Age had no significant association with CrAg ($P = 0.731$). The association between serum CrAg and CD4 count was found to be significant ($P < 0.001$). More females were CrAg-positive when compared to their male counterparts, but this difference was not statistically significant. History of past diseases such as tuberculosis, hepatitis and diabetes mellitus were not statistically significant among the patients. Exposure to risk factors such as alcohol intake, use of steroids and injection of drugs (drug abuse) was statistically significant, whereas cigarette smoking and exposure to pigeon droppings were insignificant. Although the prevalence of serum CrAg was low in this study, risk factors associated with cryptococcosis must be avoided. In addition, routine screening should be implemented to improve wellbeing and reduce morbidity. In this study we also found out that cryptococcal infection is characteristic to AIDS patients and not HIV patients as generally perceived.

Key words
Prevalence cryptococcal antigen, CrAg, serum, AIDS, HIV

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Introduction

Cryptococcus spp. is known for its capability to cause lethal fungal infections. The major cause of cryptococcosis is either *Cryptococcus neoformans* (believed to be the primary cause of human *cryptococcal* infection) or *Cryptococcus gattii*. These were initially thought to be subspecies of *C. neoformans* but have now been identified as distinct species by molecular method in 2002.[1,2] Little is known about *C.gattii* infection in Africa, where this pathogen has been isolated from both clinical and environmental samples.[3] Current knowledge on the epidemiology and clinical presentation of *C. neoformans* infection in Africa is higher compared to *C. gattii* infection.[4] Inhalation of the infectious propagule from the environment is believed to be the major mode of transmission of cryptococossis and genotypic evidence suggests acquisition can occur many years before the development of clinical cryptococcosis in the context of immunosuppression.[5,6]

Although the exact nature of the infectious propagule is unknown, the basidiospore which is created through sexual or asexual reproduction is an encapsulated, round-to-oval yeast measuring 4-6 microns with a surrounding polysaccharide capsule ranging in size from 1 to >30 microns when cultivated in the laboratory.[7] This infection occurs mainly in people with HIV or other immune compromising conditions, but rare in immune–competent individuals,[8,9] whereas *C. gattii* infection has been mainly described in apparently immunocompetent patients.[4] Cryptococcal infection is a common cause of meningitis leading to high mortality among people living with HIV/AIDS in Africa and Asia.[10,11] It is also one of the leading causes of death in patients in the first year of Antiretroviral Therapy (ART), accounting for up to 20% of deaths among AIDS patients with CD4 count < 50 cells/μL in Africa.[12] In India, *Cryptococcus* meningitis occurs in 2 - 45% of HIV positive patients.[13,14] The World Health Organization (WHO) recommends considering for

cryptococcal antigen screening and providing prophylactic therapy to those found positive for cryptococcal antigen among HIV-positive patients with CD4 count <100 cells/mm^3 in highly prevalent areas.[15] Pulmonary infection has the tendency to spontaneously resolve and is frequently asymptomatic,[16] but localized pulmonary infection may manifest as pneumonia,[8] it may disseminate to other systems of the body with a wide clinical spectrum, which may include cryptococcaemia,[17] cutaneous and oral cryptococcosis,[18] diarrhea,[19] and most commonly, central nervous system (CNS) manifestations.[1,9,16] Globally, cryptococcosis remains a remarkable cause of mortality among HIV-infected persons despite the advent of highly active antiretroviral therapy (HAART). In developed countries, the 10-week mortality in HIV patients remains high, ranging from 10-25%,[20,21] while in resource-poor countries such as Uganda, a 14-day mortality rate of 20-42% has been reported among patients with cryptococcal meningitis, despite treatment with amphotericin B.[22] In Zambia, the 6-month mortality was 100%, with a median survival of only 19 days, among AIDS patients without access to antiretroviral therapy who were treated with fluconazole. Serum cryptococccal antigen (CrAg) is a marker for invasive or disseminated cryptococcal infection and the most sensitive and specific indicator for systemic cryptococcosis.[23] A positive test therefore, warrants a search for disseminated disease. The purpose of the study was to determine the prevalence of serum cryptococcal antigen among HIV-infected patients at the University of Benin teaching hospital, using a serum CrAg lateral flow dipstick assay. We also analysed the clinical symptoms, risk factors and past history of underlying diseases in association with CrAg.

Materials and methods

Study population

This study was carried out at the University of Benin Teaching Hospital (UBTH), a 700-bed tertiary hospital located in the southern part of Nigeria, with a dedicated laboratory for HIV investigations, which is supported by PEPFAR (Presidential Emergency Plan for AIDS Relief) of the USA. Two hundred HIV-positive patients, both ART naïve and treatment experienced, within the ages of 18 and 71 years, who attended the ART clinic, were enrolled in this study. Written informed consent was obtained from each study participant and ethical approval was obtained from the Ethics and Research Committee of the UBTH. Each patient was interviewed, and a structured questionnaire was used to collect information on socio- demographic data, medical and treatment history. This information included past history on the following disease conditions: Tuberculosis, Hepatitis and *Diabetes mellitus*. History on the risk factors associated with CrAg such as exposure to pigeon droppings, alcohol intake, and smoking, use of steroids and injection of drugs was also obtained. The patients were monitored for clinical symptoms such as headache, fever, cough, nausea and vomiting, which are associated with cryptococcosis and these were also recorded in the questionnaire. The history on intake of antiretroviral and duration of ART was also obtained.

Serum cryptococcal antigen (CrAg) lateral flow assay

The CrAg lateral flow assay (Immy Immuno-Mycologics Inc, Norman, Oklahoma, USA) was further carried out, following the manufacturer's instructions. In brief, one drop of LF specimen diluent was put in a disposable micro-centrifuge tube using a pipette, 40 µl of serum was added to the reservoir and mixed, and then the white end of the cryptococcal antigen lateral flow test strip was submerged into the specimen. The result was read and recorded after 10 minutes. Double lines showed a positive result while a single line indicated a negative result.

CD_4 cell counts

The EDTA sample was used to determine CD_4 cell counts by flow cytometry (Partec, Germany) following the manufacturer's instruction. Briefly, 20 µl of whole blood was placed in a Partec tube and 20 µl of CD_4 T-cell monoclonal antibodies was added. The mixture was then incubated in the dark for 15 minutes at room temperature after which 800 µl of buffer was added. The tube was then placed in the flow cytometer for counting and the CD4 T-cell value was obtained by a programmed computer connected to the instrument.[24]

Statistical analysis

All data obtained from each patient, including results of laboratory tests were analyzed using SPSS version 22.0. CD4 count was categorized, cross-tabulated with serum CrAg results and association was determined using Chi-square. All statistical test of significance were carried out at 95% level of confidence and a P - value of < 0.05 was considered significant.[25]

Results

Two hundred HIV-positive patients were enrolled in this study and their demographic characteristics were

obtained via questionnaire as represented in Table 1. Out of 200 HIV infected patients, 180 (90%) were ART treatment experienced, while 20 (10%) were ART naïve. Four (2.2%) treatment experienced patients were positive for CrAg, while 5 (25%) ART naïve patients were positive for CrAg, which makes it a total of 9 subjects positive for CrAg as presented in Table 2. The prevalence of risk factors in relation to serum CrAg in the population such as alcohol intake (excessive intake), use of steroids, drug injection/smoking were statistically significant, while exposure to pigeon droppings and smoking were not statistically significant; disease conditions such as tuberculosis, hepatitis and diabetes mellitus were not statistically significant, as presented in Table 3. The age range of patients was between 18 years and 71 years. The difference in age prevalence in relation to CrAg was not statistically significant (P = 0.731) as presented in Table 4. In considering sex distribution in relation to serum CrAg, out of 53 males, 4 were positive for CrAg, while out of 147 females, 5 were positive for CrAg. The prevalence in sex distribution was not statistically significant (P = 0.212) as presented in Table 5. CD_4 counts of < 100 cells/µl had a higher prevalence of cryptococcal antigen, this was followed by CD_4 counts of 100-199 cells/µl and CD_4 counts of > 200 cells/µl had the least prevalence as presented in Table 6. There was a statistically significant association between cryptococcus infection and the CD_4 count of the patients <200 cells/µl (P <0.001). All the patients had at least one symptom and fever was the commonest in multivariate analysis, all these symptoms were all not statistically significant in the multivariate analysis as shown in Table 7. Headache and nausea were found to have

Table 1 Demographic characteristics of HIV patients enrolled in the study.

Age Distribution	Frequency (%)
< 20 years	1 (0.5)
20 – 29 years	21 (10.5)
30 – 39 years	70 (35.0)
40 – 49 years	56 (28.0)
50 – 59 years	38 (19.0)
60 – 69 years	12 (6.0)
70 and above	2 (1.0)
Total	200 (100)
Gender	
Male	53 (26.5)
Female	147 (73.5)
Total	200 (100)

Table 2 Determination of CrAg among ART Naïve and Treatment experienced patients.

	Treatment experienced		ART Naïve		Total No. of patients	Total CrAg positive (%)
Age (years)	No. tested	No. +ve patients (%)	No. tested	No. of +ve patients (%)		
<20	-	-	1	0 (0)	1	0 (0)
20-29	16	0 (0)	5	2 (40)	21	2 (9.5)
30-39	62	2 (3.2)	8	0 (0)	70	2 (2.86)
40-49	52	2 (3.8)	4	2 (50)	56	4 (7.14)
50-59	36	0 (0)	2	1 (50)	38	1 (2.6)
60-69	12	0 (0)	-	-	12	0 (0)
>70	2	0 (0)	-	-	2	0 (0)
Total	180	4 (2.2)	20	5 (25)	200	9 (4.5)

P = 0.786; P > 0.05

Table 3 Prevalence of risk factors and disease conditions associated with serum CrAg in the population.

Risk factors	Frequency (%) Positive	Frequency (%) Positive	**P - value**
Exposure to pigeon droppings	5 (2.5)	1 (20)	0.133
Alcohol intake	26 (13.0)	5 (19.2)	0.001
Smoking	14 (7.0)	2 (14.3)	0.090
Use of steroids	8 (4.0)	4 (50)	0.001
Smoke/ inject drugs	9 (4.5)	3 (33.3)	0.001
Diseases			
Tuberculosis	11 (5.5)	1 (90.9)	0.462
Hepatitis	4 (2.0)	1 (75)	0.089
Diabetes mellitus	5 (2.5)	1 (20)	0.133

Table 4 Age distribution of patients in relation to serum CrAg N = 200.

Age (years)	Total (%)	Negative (%)	Positive (%)	**P - value**
<20	1	1 (100)	0 (0.0)	
20 – 29	21	19 (90.5%)	2 (9.5)	
30 – 39	70	68 (97.1)	2 (2.9)	
40 – 49	56	52 (92.9)	4 (7.1)	0.731
50 – 59	38	37 (97.4)	1 (2.6)	
60– 69	12	12 (100)	0 (0.0)	
>70	2	2 (100)	0 (0.0)	
Total	200	191 (95.5)	9 (4.5)	

Table 5 Sex distribution of patients in relation to serum CrAg.

Sex	Total	Negative	Positive	**P - value**
Male	53	49	4	0.212
Female	147	142	5	
Chisquare = 1.558, **df** = 1				

significant association with serum CrAg in univariate analysis while vomiting and cough were not statistically significant. Excessive alcohol intake, use of steroids and injection of drugs were statistically significant while exposure to pigeon droppings and smoking were not statistically significant in the univariate analysis (Table 8).

Discussion

Serum cryptococccal antigen (CrAg) is a marker for invasive or disseminated cryptococcal infection and the most sensitive and specific indicator for systemic cryptococcosis.[23] A 12 ml blood sample was collected from each participant by vein puncture and an aliquot of 5 ml was put in a vacutainer bottle for serum cryptococcal antigen (CrAg) screening, using the cryptococcal antigen lateral flow assay (CrAg LFA), and another 5 ml into a container with EDTA (ethylenediamine tetracetic acid) for the determination of CD_4 cell count. Higher CD_4 count implies greater immunity against cryptococcal infection in HIV/ AIDS patients.

CrAg Lateral Flow Assay

The detection of cryptococcal capsular polysaccharide antigen (CrAg) in serum and cerebrospinal fluid using latex agglutination test (CrAg-latex) or enzyme-linked immunoassay (EIA) has been in existence for over decades.[26] They are also remarkable for better diagnosis of cryptococcal infection both in asymptomatic and symptomatic patients. In recent time the cryptococcal antigen lateral flow assay (CrAg LFA) was included as a valuable diagnostic tool for cryptococcal screening. Unlike the other tests, the CrAg LFA is a dipstick immunochromatographic assay which is very simple, rapid, low-cost test and requires no lab infrastructure. It also meets the WHO assured criteria (sensitive, specific, affordable, user-friendly, rapid and equipment- free). It has a high sensitivity for CrAg of all serotypes.[27] The CrAg LFA uses a combination of two monoclonal antibodies which allows for consistent reagent quality and performance. One monoclonal antibody is highly reactive with CrAg of serotypes A, B, and C, the second monoclonal is highly reactive with CrAg of serotypes A and D. When combined the antibodies are highly reactive with CrAg of

Table 6 Prevalence of serum CrAg in relation to CD_4 count of patients.

CD_4 count	Negative (%)	Positive (%)	Total (%)	P - value
<100	6 (54.5)	5 (45.5)	11	
100- 199	16 (88.9)	2 (11.1)	18	
> 200	169 (98.8)	2 (1.2)	171	0.001
Total	191 (95.5)	9 (4.5)	200	
Chisquare = 49.176 **df** = 2				

Table 7 Multivariate analysis.

Symptoms	Total (%)	+ve	-ve	OR	95% C.I	P
Headache	81	8 (9.9%)	73 (90.1)	0.428	0.020 - 9.147	0.587
Fever	74	9 (12.2%)	65 (87.8%)	0.000	0.000 - 0.000	0.996
Nausea	61	8 (86.9%)	53 (13.1%)	0.216	0.021- 2.189	0.195
Vomiting	6	1 (83.3%)	5 (16.7%)	0.269	0.018 - 4.001	0.340
Cough	37	4 (10.8%)	33 (89.2%)	0.204	0.030 - 1.415	0.108

Table 8 Univariate analysis.

Diseases	Total (100%)	+ve	-ve	OR	95% CI	P- value
Tuberculosis	11	1 (90.9%)	10 (9.1%)	0.442	0.050 - 3.887	0.462
Hepatitis	4	1 (75%)	3 (25%)	0.089	0.012 - 1.367	0.089
Diabetes mellitus	5	1 (20%)	4 (80%)	0.171	0.017 - 1.711	0.133
RISK FACTORS						
Exposure to pigeon droppings	5	1 (20%)	4 (80%)	0.171	0.017 - 1.711	0.133
Alcohol intake	26	5 (19.2%)	21(80.8%)	0.099	0.025 - 0.397	0.001
Smoking	14	2 (14.3%)	12 (85.7%)	0.235	0.044 - 1.255	0.090
Use of steroids	8	4 (50.0%)	4 (50.0%)	0.027	0.005 - 0.139	0.000
Smoke/ inject drugs	9	3 (33.3%)	6 (66.7%)	0.065	0.013 - 0.323	0.001
Clinical symptoms						
Headache	81	8 (9.9)	73 (90.1%)	0.077	0.009 - 0.631	0.017
Fever	74	9 (12.2%)	65 (87.8%)	0.878	0.807 - 0.956	-
Nausea	61	8 (86.9%)	53 (13.1%)	0.048	0.006 - 0.393	0.005
Vomiting	6	1 (83.3%)	5 (16.7%)	0.215	0.022 - 2.062	0.183
Cough	37	4 (10.8%)	33 (89.2%)	0.270	0.069 - 1.058	0.060

all range of cryptococcal serotypes which is an advantage over CrAg latex and EIA.[26] The CrAg LFA is highly recommended for use with Serum, plasma, or CSF for diagnosis of cryptococcal meningitis or cryptococcosis (non – meningeal) in symptomatic patients.[27] It is also used for screening of serum or plasma in ART-naïve adults with CD_4 counts less than 100 cells/mm^3 in biogeographical regions with a very high prevalence of cryptococcal antigenemia. CrAg LFA also has the capacity to detect patients with asymptomatic cryptococcal infection for urgent preemptive antifungal therapy.[27] It also has a better analytical sensitivity for *C. gattii* than CrAg- latex or EIA.[26]

In this study, CrAg LFA was used because of its efficiency in detecting cryptococcosis at an early stage both in symptomatic and asymptomatic patients. There was no need for pretreatment of sample as is always the case in Latex agglutination test.[27] The test is small, lightweight and requires no refrigeration with a long shelf life (in the case of delivery). The result was very rapid (produced in 10 minutes).

The prevalence of Cryptococcal antigen observed in this study was 4.5% among 200 HIV-positive patients. This is low compared to previous studies done in the University of Benin Teaching Hospital (UBTH), Nigeria (9.8%),[23] University of Calabar Teaching Hospital (UCTH) (13.1%),[28] and in Ethiopia (8.4%).[29] This disparity in reported prevalence could be due to the measures taken to combat this fungal infection in Nigeria since 2012, such as the majority of the patients undergo antiretroviral therapy (ART), and the patients are started on fluconazole as soon as they are positive to cryptococcal infection. Patients are also aware of the risk factors associated with this infection and they adhere strictly to the advice given to them by the physician during counseling. This study corroborates

with low prevalence of serum CrAg 2% and 5% reported in developing countries such as Vietnam,[30] and South Africa[31] respectively. This shows that the burden of cryptococcosis as an opportunistic infection in HIV-infected individuals in subSaharan Africa has been reduced drastically. The 2.2% prevalence of serum cryptococcal antigen recorded among ART treatment experienced patients in this study is low compared to 7.1% in UCTH,[32] 9.91% in UBTH[24] and 13.1% in Thailand.[33] Also a 25% serum cryptococcal antigen was observed among ART naïve patients. This finding is higher than the 12.7% prevalence reported in Benin city Nigeria[34] and 2.6% recorded among ART naïve patients in UCTH.[32] This disparity in reported prevalence could be due to the population enrolled for the study. In the UBTH and UCTH study, larger ART naïve numbers (150 and 116) were enrolled for the study while in this study only 20 persons were enrolled as ART naïve patients. The duration of ART among treatment experienced patients ranged from < 1 year to 10 years and above among the subjects, the duration of ART within 2 – 5 years recorded the highest number of patients, the patients within < 1 year to 2 years of duration of ART were those ART naïve patients newly introduced to antiretroviral therapy (ART) while those who have been on ART for 6 years and above who are supposed to have a stronger immunity against these opportunistic infections but still have a low CD_4 count (low immunity), could be due to their exposure to some ailments like diabetes, cancer e.t.c. that also reduce their CD_4 count; more attention should be paid to these patients as they are more prone to cryptococcal infection. In the prevalence of disease conditions associated with CrAg in the population, tuberculosis had 11 (5.5%) positive patients followed by diabetes mellitus 5 (2.5%) and hepatitis 4 (2.0%); these disease conditions are known to reduce immunity even though the patients are on ART. Also observed in this study was high prevalence of antigenemia (45.5%) associated with lower CD_4 counts within the range of <100 cell/µl. This is similar to previous studies done in USA,[30] and Nigeria.[24,34] This could be a result of lack of immunity against this opportunistic infection as HIV is characteristically associated with T lymphocyte depletion and is highly marked in ART naïve patients[35,36] and as also observed in this study, while a low prevalence of antigenemia (1.2%) was associated with higher CD_4 count within the range of >200 cells/µl. This is in line with previous studies done in Nigeria.[23,32] Highly active anti-retroviral therapy (HAART) has been reported to improve CD_4 counts, however patients on HAART that still have low CD_4 counts of < 200 cell/µl are at an increased risk of developing opportunistic infections which includes *Cryptococcus neoformans*. In sex distribution in relation to CrAg, more females were seropositive for CrAg when compared to their male counterparts. This could be a result of lower CD_4 count level among females than males, the female population being also higher in this study, but no statistically significant difference was found ($P = 0.212$). The majority of patients (7.1%) fell between 40-49 years of age. The difference in age

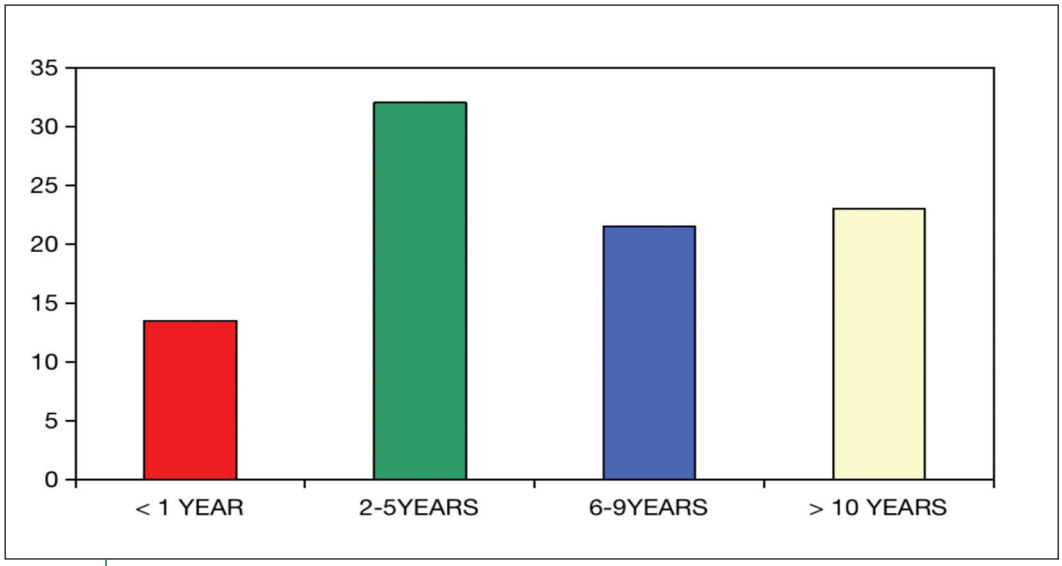

Figure 1 Duration of ART.

prevalence was also not statistically significant (P = 0.731). Risk factors associated with serum CrAg such as alcohol intake, cigarette smoking, use of steroids and drug abuse (smoked/injected drugs) had a significant association with serum CrAg in the univariate analysis while exposure to pigeon droppings was not significantly associated with serum CrAg. Clinical symptoms of CrAg were not statistically significant in association with CrAg in the multivariate analysis but they were all found to independently predict serum CrAg in a univariate analysis except for cough and vomiting which were not statistically significant (Tables 7, 8). History of disease conditions such as tuberculosis, hepatitis and diabetes mellitus were also not statistically significant in association with serum CrAg in the univariate analysis. A positive serum CrAg in a symptomatic (such as fever, nausea, headache) HIV-positive patient on ART, may imply primary cryptococcal meningitis in the background of immune suppression or immune reconstitution syndrome (IRIS) resulting from the initiation of ART, in the background of disseminated cryptococcosis. The former scenario would benefit from the management of the meningitis while the later would benefit from both meningitis treatment and IRIS treatment.

Conclusion

The low prevalence of serum CrAg among HIV- infected patients as found in this study implies that this infection has been drastically reduced in Benin city, Nigeria, due to the fact that individuals are already aware of this fungal infection and the risk factors associated with it, and the appropriate measures to combat this infection are being taken. Patients with CD_4 count <100 are more prone to cryptococcal infection. Higher CD_4 count implies greater immunity against cryptococcal infection in HIV/AIDS. ART treatment experienced patients have higher immunity against CrAg than ART naïve patients because HAART has boosted their immunity. Significant risk factors associated with serum CrAg are excessive alcohol intake, use of steroids and drug abuse as these further reduce immunity. Thus, cryptococcal antigen screening should be made a routine for all HIV-positive patients accessing care in an ART clinic. This will improve the lives of patients, reduce morbidity and prevent deaths which may arise from cryptococcal meningitis.

Περίληψη

Prevalence of serum cryptococcal antigen among HIV infected patients attending a university of Benin Teaching Hospital, Edo state, Nigeria

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Η μελέτη σχεδιάστηκε για να προσδιορίσει τον επιπολασμό του κρυπτοκοκκικού αντιγόνου ορού (CrAg) μεταξύ ασθενών με HIV λοίμωξη στο Πανεπιστημιακό Νοσοκομείο του Μπενίν (UBTH), στην πολιτεία Έντο της Νιγηρίας. Τα κλινικά συμπτώματα, οι παράγοντες κινδύνου και το ιστορικό ορισμένων ασθενειών σε συνδυασμό με το CrAg προσδιορίστηκαν σε 200 ασθενείς με HIV λοίμωξη ηλικίας 18 έως 71 ετών, χρησιμοποιώντας την ανοσοχρωματογραφία ανίχνευσης του κρυπτοκοκκικού αντιγόνου (CrAg LFA). Ο αριθμός CD4 κάθε ασθενή προσδιορίστηκε χρησιμοποιώντας το σύστημα μέτρησης BD FACS κυτταρικού διαλογέα ενεργοποιημένου με φθορισμό. Χρησιμοποιήθηκε ένα δομημένο ερωτηματολόγιο για τη συλλογή πληροφοριών σχετικά με τα δημογραφικά χαρακτηριστικά, και το ιατρικό ιστορικό των ασθενών. Το 90% των ασθενών είχαν ιστορικό λήψης θεραπείας ART και το 10% δεν είχαν λάβει ποτέ. Στη μελέτη σε 4,5% ανιχνεύθηκε κρυπτοκοκκική αντιγοναιμία. Το ποσοστό μόλυνσης ήταν υψηλότερο μεταξύ των ασθενών που δεν είχαν λάβει ART 5/20 (25%) από ό,τι στην ομάδα 4/180 που είχε λάβει θεραπεία (2,2%). Η ηλικία δεν είχε σημαντική συσχέτιση με το CrAg ($P = 0,731$). Η συσχέτιση μεταξύ της ποσότητας CrAg ορού και του αριθμού CD4 βρέθηκε να είναι σημαντική ($P < 0,001$). Περισσότερες γυναίκες ήταν θετικές στο CrAg σε σύγκριση με τους άντρες, αλλά αυτή η διαφορά δεν ήταν στατιστικά σημαντική. Το ιστορικό προηγούμενων ασθενειών, όπως η φυματίωση, η ηπατίτιδα και ο σακχαρώδης διαβήτης δεν ήταν στατιστικά σημαντικό μεταξύ των ασθενών. Η έκθεση σε παράγοντες κινδύνου, όπως η πρόσληψη αλκοόλ, η χρήση στεροειδών και η ενδοφλέβια χρήση ναρκωτικών ήταν στατιστικά σημαντική, ενώ το κάπνισμα και η έκθεση σε περιττώματα περιστεριών ήταν μη στατιστικά σημαντική. Αν και ο επιπολασμός του CrAg ορού ήταν χαμηλός στην παρούσα μελέτη, οι παράγοντες κινδύνου που σχετίζονται με την κρυπτοκόκκωση πρέπει να αποφεύγονται. Επιπλέον, θα πρέπει να εφαρμόζεται έλεγχος ρουτίνας για τη βελτίωση της υγείας και τη μείωση της νοσηρότητας. Σε αυτή τη μελέτη βρέθηκε επίσης ότι η κρυπτοκοκκική λοίμωξη αφορά ασθενείς με AIDS και όχι ασθενείς με HIV, όπως γενικά γίνεται αντιληπτό.

Λέξεις κλειδιά
Επιπολασμός κρυπτοκοκκικού αντιγόνου, CrAg, ορός, AIDS, HIV

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