Spectrum of Comorbid Conditions and Their Relationship to CD4 T-lymphocyte Counts in HIV-Infected Patients in Mbour, Senegal

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Background: Individuals infected with the human immunodeficiency virus (HIV) and Acquired Immunodeficiency Syndrome (AIDS) present with a broad spectrum of clinical conditions as a result of compromised immune systems. There is little data reflecting the clinical spectrum and prevalence of comorbid conditions among HIV/AIDS patients in Mbour, Senegal.

Objective: This study aims to describe the incidence of comorbidities affecting HIV/AIDS patients in Mbour and to examine the relationship between comorbidities and CD4 T-lymphocyte counts in this population.

Materials and Methods: We conducted a retrospective chart review of patients seeking care for HIV/AIDS at the Hospital of Mbour (n=426) between March 2005 and May 2014. CD4 counts at presentation and comorbid conditions were documented and analyzed to determine frequency of each condition in the population and the relationship between CD4 counts and clinical presentation of disease.

Results: The most common condition in patients with HIV/AIDS at presentation in Mbour is chronic diarrhea (30.7% of patients), followed by dermatitis (29.5%) and oral candidiasis (25.4%). Patients presenting with candida infection, dermatitis and diarrheal illness have significantly lower CD4 counts than those presenting without these conditions. Patients with CD4 counts below 200 cells/μL have a greater number of comorbidities than patients with higher CD4 values.

Conclusion: This study outlines the clinical profiles of patients presenting with HIV/AIDS at the Hospital of Mbour and correlates symptoms with CD4 counts. This data could be utilized clinically to promote community educational outreach for early detection of disease based on the most common presentation of HIV/AIDS in this patient population.

Introduction

The HIV/AIDS pandemic has been at the frontline of public health interest in sub-Saharan Africa for the past thirty years. Despite the global media's focus on the AIDS crisis, there are persistent barriers to the eradication of the disease in many regions. These barriers include increasing poverty and limited access to basic health care for many of the poor and middle income residents of African countries like Senegal.[1] AIDS activists have drawn attention to the global disparities in access to technologies for HIV prevention, testing and treatment as well as impediments to access to primary health care or other health related resources. While great strides have been made in areas of universal access to treatment, many disparities persist as obstacles to effective disease prevention and detection.[1]

In the 1980s, the Senegalese government was one of the first African governments to acknowledge the HIV/AIDS pandemic and began to aggressively address this issue through education campaigns and blood screening.[2] At this time, the government made a financial commitment to universal access to HIV/AIDS treatment. Today these treatments are still offered free of charge, by there has been only a modest decrease in the prevalence of HIV/AIDS in Senegal: From 0.6% in 2005 to 0.5% in 2015.[2] The estimated number of individuals living with HIV in Senegal in 2015 was 46,000, with 1,600 new HIV infections over the past year and 2,200 AIDS related deaths over the past year.[3] Despite government subsidization of treatment, only 18,375 of the 46,000 (40%) individuals living with HIV were receiving antiretroviral treatment in 2015.[3] An estimated 36% percent of pregnant women living with HIV received antiretroviral treatment to prevent mother-to-child transmission in 2015.[3] These numbers reflect the discordance between the aims of the global health community in universal treatment access and the reality of antiretroviral treatment status of many individuals in Senegal. The reason for the failure of such treatment programs is unknown. It should be noted that even though the prevalence of HIV/AIDS in Senegal has not decreased significantly since treatment reforms, it is still very low compared to the rest of Sub-Saharan Africa, where disease rates are as high as 28%.[4]

"Treatment 2015" is a Joint United Nations Program on HIV/AIDS (UNAIDS) initiative focusing on expediting progress towards universal treatment access. The initiative calls for innovative thinking in HIV counseling and encourages countries to establish national testing in order to facilitate earlier access to services.[5] This initiative acknowledges that the first step in increasing treatment efficacy involves increased knowledge of HIV status, which requires more widespread diagnostic efficiency. However, laboratory diagnosis of HIV in Mbour, Senegal is not always readily available due to the paucity of laboratories. In addition, such diagnostic testing must be paid for out of pocket. Given the financial and geographical barriers to laboratory testing for HIV status, recognizing HIV infection by its clinical manifestations in order to prompt a more thorough diagnosis and to ensure proper treatment when indicated remains essential.

The stage at which HIV is diagnosed is crucial, as earlier diagnoses are associated with improved patient survival, reduced direct care costs and lower rates of onward transmission.[6] Furthermore, early

and accurate recognition of HIV is vital to public health initiatives to eradicate the disease, as the risk of transmission increases eight to ten-fold during the acute phase of infection, defined as the six-month period following HIV acquisition when compared to the chronic phase.[6] Early initiation of treatment can reduce progression to AIDS.[7] However, clinical diagnosis of HIV-related conditions in the primary care setting is complex, as many of the presenting signs or symptoms associated with HIV are seen in individuals without HIV. Early HIV infection may manifest with symptoms including fever, fatigue, skin rash, diarrhea and weight loss.[8] Most symptoms of early infection are transient and relatively nonspecific. Moreover, even laboratory tests may not detect the immune system's antibody response during this phase.[9]

An important biological marker of HIV-related immunosuppression is the reduction of CD4 T-lymphocyte counts. The CD4 T-lymphocyte is an important coordinator of many immunologic functions. HIV selectively targets and infects CD4 T-lymphocytes, resulting in functional impairment and death of these cells. As the number of CD4 T-lymphocytes decreases, the risk and severity of comorbid conditions increases. Therefore, it is important to understand and recognize the specific comorbidities common to the HIV/AIDS population in Mbour in order to accurately diagnose and treat the disease as early as possible. A study performed in the United Kingdom by Damery et al. revealed that the conditions most strongly associated with subsequent HIV diagnosis were bacterial pneumonia, oral candidiasis, herpes zoster, weight loss, pyrexia of unknown origin and diarrhea.[10] An improved awareness of common disease manifestations specific to patients in Mbour, Senegal, may contribute to the efficacy of diagnosis and disease eradication in this region.

This study aims to outline the clinical spectrum of HIV-related disease at the Hospital of Mbour and to examine the relationship between presenting comorbidities and CD4 T-lymphocyte counts in this patient population. We hypothesized that CD4 counts would be lower in the patients presenting with comorbid disease when compared with patients without comorbid disease and that patients presenting with lower CD4 counts would display a greater number of comorbidities.

Table I: Frequency of comorbid conditions

Condition	Present		Absent	
	%	N	%	N
Candida of the mouth	25.4	107	74.6	314
Candida of the esophagus	12.6	53	87.4	368
Chronic diarrhea	30.7	129	69.3	291
Herpes	9.7	41	90.3	290
Pruriginous dermatitis	29.5	124	10.5	297
Sarcoma	0.24	1	99.8	420
Seborrheic dermatitis	0.71	3	99.3	417
Shingles	6.6	28	93.4	393
Tuberculosis	14.25	60	87.75	361

Method

Setting

This study took place at the Hospital of Mbour, a regional hospital in Senegal, West Africa. The Hospital of Mbour is a regional medical facility in the Thiès region of Senegal, which is located at the western border of the country. The Hospital of Mbour serves an area of over 500,000 people, has approximately 80 inpatient beds, 29 maternity beds and 140 medical staff, as measured by the researcher and collaborating physician. The hospital complex provides both ambulatory and inpatient care, and is affiliated and administered by the University of Thiès Medical School. While there are several smaller medical facilities in the Thiès region, the Hospital of Mbour is the only regional hospital with a government-funded AIDS treatment program. The hospital participates in a medical exchange program, allowing students from the United States to learn from the caregivers and patients in Mbour. In exchange, physicians from The Hospital of Mbour visit a hospital in the United States. This study was completed by a medical student from the United States in collaboration with a physician from The Hospital of Mbour as a means of quantifying years of data from paper charts.

Sample

The sample includes all charts from patients who were diagnosed with HIV or AIDS between March 2005 and May 2014 and who received care at the hospital facility.

Measures

Information was collected regarding age, gender (male or female), marital status (married, divorced, or single), CD4 count at presentation and presence or absence of nine individual comorbidities: tuberculosis, candidiasis of the mouth (fungal infection of the oral membranes), candidiasis of the esophagus (fungal infection of the esophagus), pruritic dermatitis (skin lesions with intense itching), herpes zoster (viral infection causing shingles), herpes simplex (viral infection causing ulcers), Kaposi sarcoma (a rare cancer due to a subtype of the herpes virus), seborrheic dermatitis (skin condition causing scaly patches) and chronic diarrhea. These nine comorbidities were the conditions outlined by the HIV/AIDS-specific charts, which have been utilized by the Hospital of Mbour since March 2005. These charts were organized and implemented in an attempt to better consolidate and record information about the HIV/AIDS patients who were diagnosed and treated at the Hospital of Mbour. This study was approved by ethics review boards at the lead author's institution with a letter of permission and support from the Hospital of Mbour. The lead researcher, with assistance from the head of Internal Medicine and director of the HIV program, developed the chart abstraction protocol, performed the chart review, and interpreted the results. There was no direct patient contact specific to the study as only existing data were used in our analysis.

Analytical approach: Descriptive statistics were employed to describe the distribution of demographic and clinical factors. The mean and standard deviation are provided for continuous variables and the frequency and number of patients in each category are provided for discrete variables (Table I). The percentage of patients presenting with each of the comorbidities was analyzed and reported as frequency and number of patients (Table II).

A two-tailed independent sample t-test was employed to assess the average CD4 count of patients in relation to comorbidity status (Table III). CD4 was dichotomized as CD4 >200 cells/μL and CD4 <200 cells/μL, with the latter indicating AIDS defining illness. T-tests were used to examine the relationship between the quantitative sum of comorbidities for any individual and AIDS-defining illness (Table III).

Results

The sample analyzed in this study includes 426 patients who received treatment for HIV/AIDS at the Hospital of Mbour. Data was collected from the first day that the individuals became patients at the Hospital of Mbour. The average age of presentation is 41 years and the average CD4 count at presentation is 295.8 cells/μL. There are 296 (69.5%) female and 130 (30.5%) male patients. Of the patients with HIV/AIDS, 53 (15%) are single, 225 (63.6%) are married and 74 (20.9%) are divorced. There are 74 charts missing data on marital status.

Table I reflects the frequency of each comorbid condition. The most common condition in patients with HIV/AIDS at presentation was chronic diarrhea (30.7% of patients), followed by pruritic dermatitis (29.5%) and candida of the mouth (25.4%). N reflects the number of patients with each comorbidity. Some charts were missing data regarding the presence or absence of the comorbidities, resulting in

Table II: CD4 mean

Condition (cells/μL)	Present	Absent	p-value	t-value
Candida of the mouth	228.8	320.8	0.0035*	2.94
Candida of the esophagus	176.5	312.4	<0.0001*	5.42+
Chronic diarrhea	205.5	336.7	<0.0001*	5.31+
Herpes	259.4	299.9	0.399	0.84
Pruriginous dermatitis	229.9	324.9	0.0004*	3.58+
Sarcoma	---	---	---	---
Seborrheic dermatitis	---	---	---	---
Shingles	240.8	299.6	0.115	1.63+
Tuberculosis	252.6	301.6	0.128	1.54+

*: p<0.05 according to student's t-test

---: Only 1 case had Sarcoma and 3 had Seborrheic dermatitis and as a result, t-values could not be calculated

+: Results from t-test using Satterwaite correction for inequality in variance

Table III: CD4 count and presence of comorbid conditions

	CD4>200	CD4<200	p-value	t-value (DF)
Mean number of comorbidities	1.0517	1.4735	0.0033*	-2.96

*: p<0.05 according to t-test

an incomplete count in each category.

Table II lists the mean CD4 count for patients presenting with and without the nine comorbid conditions included in this study. Patients presenting with candida of the mouth, candida of the esophagus, pruritic dermatitis and chronic diarrhea had significantly lower CD4 counts than those presenting without these conditions.

Table III lists the mean number of comorbidities present in patients with CD4 counts above and below 200 cells/μL. Patients with CD4 counts below 200 cells/μL presented with an average of 1.4735 comorbid conditions, while patients with CD4 counts above 200 cells/μL presented with an average of 1.0517 comorbid conditions. This is a significant finding (p= 0.0033), indicating that lower CD4 counts are correlated with a greater number of comorbid conditions in this patient population.

We hypothesized that CD4 counts would be lower in the patients presenting with comorbid disease when compared with patients without comorbid disease. The results listed in Table II reveal that patients presenting with candida of the mouth and esophagus, pruritic dermatitis and chronic diarrhea had significantly lower CD4 counts than patients presenting without these comorbidities. We also hypothesized that patients presenting with lower CD4 counts would display a greater number of comorbidities. The results listed in Table III show that patients with CD4 counts below 200 cells/μL are inflicted with a greater number of comorbidities than patients with higher CD4 values.

Concluison and Discussion

These results give insight into the clinical profiles of the patients with HIV/AIDS at the Hospital of Mbour, information that may be used to improve early detection of HIV symptomatology within the community or in the primary care setting. Our findings outline the most common comorbidities that are present at the onset of HIV infection in this patient population, including chronic diarrhea, dermatitis and oral candidiasis. This data may be useful for illustrating the common clinical picture of a patient with HIV/AIDS in a resource-poor environment, where additional laboratory testing is not readily available and physical examination is the primary diagnostic tool. In addition, these conditions could serve as useful indicators that prompt patients experiencing such symptoms to seek appropriate diagnostic workup. Furthermore, they could also be utilized as a focus of educational outreach to encourage community members to seek care as soon as such symptoms arise.

A number of studies examining comorbid conditions in HIV/AIDS have found data consistent with our findings. A study by Ramphoma et al. revealed that at least 70% of the people living with HIV/AIDS in Lesotho presented with oral manifestations of HIV as the first sign of disease. The majority (91.3%) of these cases are oral candidiasis, while other lesions found include Kaposi's sarcoma and oral hairy leukoplakia.[11] Okoh et al. observed that orofacial lesions were among the earliest clinical manifestations of HIV infection in Nigerian women, with 57% of patients presenting with oral lesions. Of these, oral candidiasis was the most common, with 37.8% affected, followed by melanotic pigmentation and xerostomia.[12]

Additional studies have investigated the prevalence of head and neck, ocular and hematological manifestations of disease. A study by Tshifularo et al., describing HIV-infected patients in South Africa, revealed that the most common manifestations were adenoid hyperplasia, cervical lymphadenopathy and chronic suppurative otitis media.[13] Bekele et al. outlined the most common ocular manifestations of HIV/AIDS in Ethiopia and found that the overall prevalence of ocular manifestations was 25.3%, with keratoconjunctivitis sicca (dry eyes) being most common.[14] Munyazesa et al. found that 4.2% of HIV-positive Rwandan women studied had marked anemia (Hb <10.0 g/dl), while none of the HIV-negative women had any degree of anemia. The degree of anemia was highest in HIV-positive women with CD4 <200 cells/mm.[2,15]

Our study revealed that patients with dermatitis had significantly lower CD4 counts than those presenting without these conditions. Boonchai et al. observed that 75% of HIV patients in Thailand with popular pruritic eruption (PPE) had an advanced degree of immunosuppression with CD4 counts below 50mm.[2,16] PPE is characterized by chronic pruritis on the trunk and extremities not explained by other causes and is the most common cutaneous manifestation in HIV infected patients.[16] Our results

support the hypothesis that pruritis may be regarded as a cutaneous marker of advanced HIV infection and used to predict the CD4 count in these patients, determine need for treatment and monitor response to treatment.

Candida infection among our sample was similarly associated with lower CD4 counts. Badiane et al. quantified the prevalence of opportunistic fungal diseases in the general population in Senegal, indicating that conditions such as candidemia, invasive aspergillosis, mucormycosis and histoplasmosis are likely underestimated due to lack of clinical suspicion and diagnostic test availability.[17] The authors suggest that fungal opportunistic infections are likely more common than the data shows, with diagnosed cases representing only a small fraction of the disease burden. Badiane et al. demonstrated that over a period of a year, 90% of those with AIDS defined as having a CD4 count below 200 cells/μL develop oral candidiasis. Our results showed a 25.4% prevalence of oral candidiasis at the time of presentation, but are limited in predicting the point prevalence and overall prevalence of disease due to the design of the study.

The most common comorbid condition present in our sample was chronic diarrhea (30.7%) and patients presenting with diarrheal illness had decreased CD4 counts compared with patients without this comorbidity. Rubaihayo et al. reported chronic diarrhea as one of the most common complications of HIV in a study analyzing the effects of treatment on prevalence of diarrheal disease. The study demonstrated a decline in diarrhea prevalence from 12% in 2002 before highly active antiretroviral therapy (HAART) availability to 2% in 2013 with the advancement of HAART availability in Uganda.[18] This study addresses the major negative impact of chronic diarrhea on quality of life for patients infected with HIV and also points out the effectiveness of HAART on combating the comorbidities of HIV infection with a significant reduction in prevalence with the onset of increased access to therapy.

The massive global expansion of access to HIV treatment has been promising, with 9.7 million people receiving HAART in low and middle-income countries in 2012 compared with 300,000 in 2002.[19] However, there are geographical variations in this success. As of December 2012, at least 80% of individuals with HIV were not receiving therapy, with the most dramatic gaps in treatment occurring in Western and Central Africa.[20] Our study analyzed the prevalence of comorbidities among all patients presenting with HIV from 2005 to 2014. Further research could analyze variations in patterns of disease presentation with time to evaluate the effectiveness of HAART therapy in this particular region.

This study was limited in the use of retrospective chart review to obtain data. The charts used by the Hospital of Mbour for patients with HIV included areas for documentation of only the comorbid diseases listed in Table II, limiting the results of this study to focus on these specific conditions. There are a vast number of clinical events defined by the WHO for clinical staging and classification not listed in this study, including persistent fever, anemia, pneumocystis pneumonia, HIV encephalopathy and molluscum contagiosum infection.[19] Further research might include identification of common conditions not listed on the routine charts used at the Hospital of Mbour. Further collaboration with the Hospital of Mbour might focus on expanding the criteria used to diagnose HIV/AIDS based on clinical presentation.

An additional limitation of the present study concerns the use of data present at patient presentation to the Hospital of Mbour. Due to the limited access to hospital care for patients in rural regions of Senegal, it is difficult to confirm the exact point in disease progression in which the patients initiated care at the Hospital of Mbour. It is not known whether patients sought care immediately after the onset of concerning symptoms, or if disease had been present for months or years before the initial visit to the hospital.

Further research might focus on identifying barriers to obtaining laboratory testing in the initial stages of HIV diagnosis in order to facilitate earlier diagnosis and better diagnostic outcomes. In addition, outreach programs focusing on educating members of the community about the common symptoms of HIV/AIDS may be implemented as a means of increasing the number of patients who are recognized and treated at early stages of disease.

A study by Lewden et al. that aimed to describe the causes of mortality in HIV-positive adults hospitalized in West Africa found that the most frequent fatal diseases were tuberculosis (36%), cerebral toxoplasmosis (10%) and cryptococcus (9%).[19] The study concluded that sustained efforts are needed to optimize earlier diagnosis of HIV infection and initiation of treatment. A goal of the present study is to expand the understanding of clinical presentations to enhance early diagnosis of HIV.

The results of this study reveal that the most common condition in patients with HIV/AIDS at presentation in Mbour is chronic diarrhea (30.7% of patients), followed by dermatitis (29.5%) and oral candidiasis (25.4%). Patients presenting with candida infection, dermatitis and diarrheal illness have significantly lower CD4 counts than those presenting without these conditions and patients with CD4 counts below 200 cells/μL present with a greater number of comorbidities than patients with higher CD4 values.

With very little existing data on the clinical presentation of HIV/AIDS patients in Mbour and Senegal as a whole, it is our hope that this study will increase the pool of available knowledge on this subject. In addition, the clinical comorbidities discussed in this study may be used as an indicator of disease to prompt patients to seek diagnostic workup for earlier detection of disease.

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