E-ISSN: 2378-654X

Recent Advances in Biology and Medicine

Original Research Article

Clinical Correlates of Diarrhea and Gut Parasites among Human Immunodeficiency Virus Seropositive Patients

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Clinical Correlates of Diarrhea and Gut Parasites among Human Immunodeficiency Virus Seropositive Patients

Elvis Bisong*, Ndifreke Udonwa, Abraham Gyuse, Ita Okokon, Emmanuel Monjok
Department of Family Medicine, Faculty of Medicine, College of Medical Sciences, University of Calabar, Calabar, Nigeria.

***Correspondence:** drelvo@yahoo.com

Received: May 17, 2017; Accepted: Sep 18, 2017

Abstract
Cluster differentiation 4 (CD4) count estimation, which is not readily available in most resource poor settings in Nigeria, is an important index-determining commencement of antiretroviral therapy (ART). It is imperative for physicians who come in contact with these patients in such settings to recognize other parameters to evaluate these patients. The clinical correlates of diarrhea and gut parasites among human immunodeficiency virus (HIV)-seropositive patients attending our special treatment clinic were studied. Three hundred and forty consenting HIV-positive adult subjects were enrolled. Their stool and blood specimens were collected for a period of three months. Stool samples were analyzed for the presence of diarrhea and gut parasites. The patients were clinically evaluated by physical examination for the presence of pallor, dehydration, oral thrush, wasting lymphadenopathy, dermatitis, skin hyperpigmentation, and finger clubbing. Participants with diarrhea represented 14.1% of the population, while 21.5% harbored one or more parasites. In the subjects with diarrhea, 14.6% harbored gut parasites. The presence of diarrhea was associated with a low CD4 count. Clinically, oral thrush, wasting, and rashes were more reliable predictors of low CD4 count levels; whereas, the presence of pallor, dehydration, wasting, and rashes correlated with the presence of diarrhea. HIV patients presenting with pallor, dehydration, wasting, and rashes should be evaluated for the presence of diarrhea. The clinical variables associated with low CD4 count in this study may guide commencing antiretroviral therapy in resource poor settings.

Keywords: HIV; Resource poor settings; Diarrhea; Gut parasites.

1. INTRODUCTION

The human immunodeficiency virus (HIV) infection leads to a gradual depletion and suppression of the immune system. This results in an increased susceptibility of the body to infections and can ultimately cause acquired immune deficiency syndrome (AIDS). Most people infected with HIV do not know that they have become infected. This is because they may be symptomless after the initial infection; however, they are highly infectious and can transmit the virus to other people [1].

Diarrhea disease has been shown to be the commonest presentation of AIDS in Africa [2]. It occurs in nearly 90% of patients with advanced HIV infection in central Africa compared with 30-60% in developed countries [3]. In Nigeria, chronic diarrhea is a very common presentation in HIV infection [4-6] with a prevalence of 61% [4].

The presence of diarrhea in patients with HIV infection may be associated with some conditions which include infection with conventional and opportunistic microorganisms [7, 8], enteropathy, malignancy, and even treatment with various agents. Thus, HIV-related diarrhea disease has been linked to multifactorial etiopathogenesis with enteric parasites possibly playing a prominent role.

The broad clinical spectrum of diseases owing to intestinal parasites in HIV patients vary from asymptomatic infestation to severe, life threatening diarrhea, dehydration, and malabsorption [9].

Various factors have been attributed to the disproportionate impact of HIV in resource poor settings. These include poverty, disease stigma, cultural and social barriers to testing and treatment, insufficient health care infrastructure to support a large patient pool, and lack of health literacy [10]. Other factors are limited provider training, inadequate medical equipment, and paucity of manpower with few qualified laboratory facilities [10]. In areas with adequate resources, the laboratory measurements of cluster differentiation 4 (CD4) cells and plasma HIV viral load are commonly used to determine the degree of immunosuppression and the rate of destruction of the immune system in HIV patients [11]. These tools are used to evaluate the eligibility for treatment and to monitor disease progression. With scarce resources to test CD4 cell counts and plasma HIV viral load in resource poor settings, clinicians may rely on clinical parameters when assessing the disease status of the patient.

By establishing a relationship between the presence of diarrhea, gut parasites, and clinical state of these patients with the level of CD4 count, an algorithm may be provided with which it may be possible to initiate antiretroviral therapy without CD4 count estimation in HIV-seropositive patients in resource poor settings. Furthermore, by identifying the agents responsible for diarrhea, it may be possible to initiate specific treatment.

The primary objective of this study was to determine the clinical correlates of diarrhea and gut parasites among HIV-seropositive patients attending the special treatment clinic of a University Teaching Hospital in a developing country.

2. METHODS

This was a descriptive cross-sectional hospital-based study conducted in the adult Special Treatment Clinic (STC) of the University of Calabar Teaching Hospital (UCTH), in Cross River State, Nigeria. Ethical clearance was obtained from the Ethical Committee of UCTH before commencement of the study. The inclusion criteria included patients who were confirmed to be HIV seropositive at the STC who gave written consent for the study.

A researcher administered proforma form documenting the participants' sociodemographic characteristics, clinical findings, CD4 count, presence of diarrhea, and highly active antiretroviral therapy (HAART) status was issued. The subjects were clinically evaluated by physical examination for pallor, dehydration, oral thrush, wasting, peripheral lymphadenopathy, dermatitis, skin hyperpigmentation, and finger clubbing**.** The diagnosis of HIV was made following standard protocol that involved voluntary counseling and testing. The CD4 count of the enlisted subjects was analyzed using the automated flocytometry method. Fresh stool samples were collected using wide-mouthed plastic containers. The physical appearance of each stool sample was noted. The stools were analyzed for the presence of parasites by a trained laboratory scientist using the flotation method.

Data was precoded and double-entered for accuracy using the Statistical Package for Social Sciences version 15 software (SPSS 15). A p-value of less than 0.05 was taken as significant.

3. RESULTS

Three hundred and forty subjects were recruited for the study. There were 242 (71.2%) females and 98 (28.8%) males. The mean CD4 count value was 314 with a median range of 5-1610. A total of 239 subjects representing 70.3% of the study population were on antiretroviral therapy. Table 1 shows the sociodemographic characteristics of the study population.

Two hundred and ninety two subjects representing 85.9% subjects had no diarrhea; whereas, forty eight subjects representing 14.1% presented with diarrhea during the study period. Twenty eight persons representing 58.3% of the subjects with CD4 count less than 200 had diarrhea; whereas, 41.7% of those with CD4 counts of 200 and above had no diarrhea. The pattern of diarrhea was less than two weeks for 39.6% of subjects with diarrhea; whereas, 60.4% had diarrhea of two weeks and above. Forty (83.3%) of those with diarrhea had a diarrhea frequency of 3-6 times daily, and 8 (16.7%) had a diarrhea frequency of greater than 6 times daily. The higher the CD4 value, the lower was the frequency of diarrhea, as shown in Figure 1.

Two hundred and sixty seven subjects representing (78.5%) subjects had no parasites identified in their stool samples (Table 2). Seventy three (21.5%) had various parasites identified in their stool samples.

Seven respondents constituting 14.6% of those with diarrhea-harbored gut parasites; whereas 41 (85.4%) of those with diarrhea had no identifiable parasites in their stool.

In analyzing the relationship between clinical status and CD4 count, there was statistical significance in subjects with pallor, dehydration, oral thrush, diarrhea, physical wasting, dermatitis, rashes, finger clubbing, and skin hyperpigmentation. There was no statistical significance in subjects who harbored gut parasites. Using the multivariate logistic regression model, statistical significance was noted in respondents with oral thrush, physical wasting, and rashes (Table 3).

Analyzing the relationship between clinical status and diarrhea, there was statistical significance in the studied population for pallor, dehydration, wasting, rashes, and finger clubbing. There was no statistical significance for oral thrush, dermatitis, hyperpigmentation, and gut parasites. There was statistical significance for pallor, wasting, rashes, and dehydration using multivariate analysis (Table 4).

There was no statistical significance for any of the variables both independently and when considered jointly to buttress a relationship between clinical status and gut parasites.

4. DISCUSSION

In this study, most of the respondents were of the 20-49 years age group constituting 87.1% of the studied population. Majority of the patients in this study belonged to the active working population in the prime of their lives. Most persons between the ages of 15 and 49 years are sexually active. The age group findings in this study were in good agreement with the UNAIDS/WHO report on the global HIV/AIDS epidemic update of 2008 [12].

Table 1: Sociodemographic characteristics of respondents.

Age	Frequency	Percentage
<20	6	1.7
20-29	110	32.4
30-39	118	34.7
40-49	68	20.0
50-59	34	10.0
≥60	4	1.2
TOTAL	340	100.0
Gender		
Female	242	71.2
Male	98	28.8
Total	340	100.0
Marital status		
Divorced	21	6.2
Married	155	45.6
Single	124	36.5
Widowed	40	11.8
Total	340	100.0
Occupation		
Trader	112	32.9
Farmer	23	6.8
Student	29	8.5
Civil servant	67	19.7
Artisans	109	32.1
Total	340	100.0
Religion		
Christianity	335	98.5
Islam	5	1.5
Total	340	100.0
Education level		
Nil	22	6.5
Primary	89	26.2
Secondary	133	39.1
Tertiary	96	28.2
Total	340	100.0
Source of drinking water		
Stream	42	12.4
Bole hole	251	73.8
Tap	41	12.1
Others	6	1.8
Total	340	100.0
Residence		
Urban	244	71.8
Rural	96	28.2
Total	340	100.0
Sewage disposal		
VIP	138	40.6
Bush	14	4.1
Shank	87	25.6
Pit latrine	101	29.7
Total	340	100.0

Figure 1: Graph of CD4 count versus diarrhea frequency. *N* = 340.

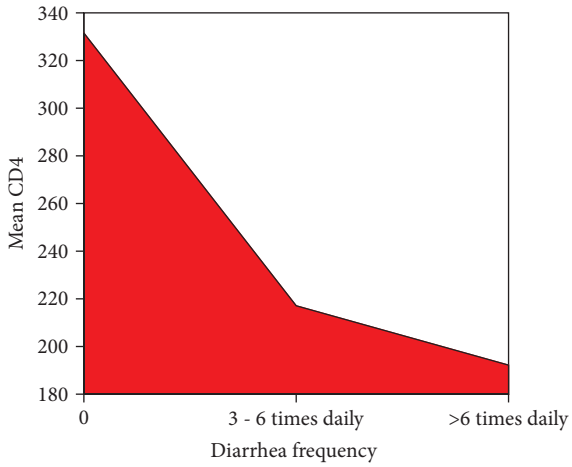

Table 2: Parasite distribution among respondents *N* = 340.

Variable	Frequency	Relative frequency (100%)
Type of parasites		
No parasite	267	78.5
Ascaris lumbricoides	37	10.9
Hookworm	16	4.6
E. coli	3	0.9
Flagellates of protozoa	1	0.3
Mixed (ascaris + *E. coli)*	2	0.6
Mixed (ascaris + hookworm	10	3.0
Mixed (*E. coli* + *T. trichiuria*)	1	0.3
Mixed (ascaris + *E. coli* + *T. trichiuria*)	1	0.3
Mixed (hookworm + ascaris + trichuris)	2	0.6
Total	340	100%

The greater number of respondents in this study being women was in agreement with similar studies [13-15]. There are biological, sociocultural, and economic factors that predispose women to HIV acquisition more than their male counterparts.

The observed proportion of study subjects who presented with diarrhea was 14.1%. This agrees well with a similar study where the prevalence of diarrhea ranged from 0.9 to 14% in HIV outpatients [16]. However, our study value is low when compared to similar studies with the prevalence rates of 30.6 and 57.44%, respectively [17, 18] The comparatively low value found in this study may be attributed to the fact that majority (70.3%) of the respondents were already on antiretroviral therapy, which may have improved their immune function.

Out of the three hundred and forty subjects who met the inclusion criteria for this study, 21.5% harbored one or more forms of intestinal parasites. Compared to similar studies, this value was higher (8.7, 15.3%) [19, 20], slightly lower (26. 29.8, 28.1%) [18, 21, 22], and lower (30, 51.4, 69.2, 79.3%) [23-26] prevalence rates.

Variations in the prevalence rate of intestinal helminthiasis from different communities may be due to people's level of education, standard of personal/environmental hygiene, and perhaps social habits. Some factors such as temperature, relative humidity, rainfall, and different diagnostic techniques employed by various workers may be responsible for the observed differences in prevalence between communities.

In conformity with similar studies [27, 28], majority of the subjects with diarrhea had the chronic type. However, a similar study had more participants with acute than chronic diarrhea [29] in contrast to our study findings.

It was observed in this study that the diarrhea frequency reduced with improved CD4 count values. This may be attributable to improved immune function. Diarrhea was common and strongly associated in patients with low CD4 cell count.

Table 3: Relationship between CD4 count and clinical status.

Variable	CD4 count of patients (*n* = 340)			
	Univariate logistic regression		Multivariate logistic regression	
	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
Pallor				
No	1	0.003	1	0.698
Yes	4.33 (1.62; 11.59)		0.75 (0.18; 3.21)	
Dehydration				
No	1	0.040	1	0.985
Yes	3.22 (1.05; 9.82)		0.99 (0.20; 4.84)	
Oral thrush				
No	1	<0.0001	1	0.002
Yes	4.27 (2.32; 7.83)		3.11 (1.52; 6.38)	
Diarrhea				
No	1	0.001	1	0.603
Yes	2.77 (1.49; 5.17)		1.25 (0.55; 2.85)	
Wasting				
No	1	<0.0001	1	<0.0001
Yes	13.87 (5.64; 34.07)		8.58 (2.77; 26.58)	
Dermatitis				
No	1	0.022	1	0.458
Yes	3.60 (1.20; 10.80)		1.64 (0.44; 6.08)	
Rashes				
No	1	<0.0001	1	<0.0001
Yes	5.37 (3.04; 9.49)		5.08 (2.71; 9.55)	
Finger clubbing				
No	1	0.001	1	0.474
Yes	8.79 (2.47; 31.23)		1.89 (0.33; 10.68)	
Hyperpigmentation				
No	1	<0.0001	1	0.516
Yes	3.96 (1.90; 8.24)		1.36 (0.54; 3.43)	
Gut parasites				
No	1	0.988	***	***
Yes	1.00 (0.58; 1.70)			

***Not significant in the univariate logistic regression model.

This finding is in agreement with similar studies [30-32]. In addition, HIV patients may be prone to oxidative stress that may contribute to the process of diarrhea and a study conducted in Tunisia among the general population has shown that the oxidative stress is associated with gastrointestinal disturbances including diarrhea [33]. Oral thrush, wasting, and rashes were associated with a low CD4 cell count. These findings were replicated in similar studies [34-36].

The direct and flotation methods used in this study have the limitation that some parasites cannot easily be diagnosed with this method. Reliance on participants report to assess symptoms and duration of diarrhea may have introduced bias.

5. CONCLUSION

Oral thrush, wasting, and rashes were the most predictive clinical variables associated with a low CD4 count. The higher the CD4 count the lower the frequency of diarrhea. Clinically, the presence of pallor, dehydration wasting, and rashes together predicted the presence of diarrhea in this study. There were no clinical correlates observed with the presence of gut parasites in this study.

Acknowledgement
We are grateful to all the staff of the Special Treatment Clinic for their support during the study period.

Table 4: Relationship between clinical status and diarrhea.

Variable	Diarrhea (n = 340)			
	Univariate logistic regression		Multivariate logistic regression	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Pallor				
No	1	<0.0001	1	0.028
Yes	9.35 (3.63; 24.06)		3.72 (1.15; 12.04)	
Dehydration				
No	1	0.001	1	0.004
Yes	6.95 (2.32; 20.83)		7.26 (1.87; 28.11)	
Oral thrush				
No	1	0.089	***	***
Yes	1.88 (0.91; 3.89)			
Wasting				
No	1	<0.0001	1	0.013
Yes	6.70 (3.27; 13.74)		3.37 (1.29; 8.81)	
Dermatitis				
No	1	0.164	***	***
Yes	2.32 (0.71; 7.62)			
Rashes				
No	1	<0.0001	1	0.001
Yes	3.46 (1.81; 6.62)		3.31 (1.61; 6.80)	
Finger clubbing				
No	1	0.015	1	0.371
Yes	3.65 (1.28; 10.39)		0.52 (0.13; 2.17)	
Hyperpigmentation				
No	1	0.052	***	***
Yes	2.27 (0.99; 5.17)			
Gut parasites				
No	1	0.214	***	***
Yes	0.58 (0.25; 1.36)			

***Not significant in the univariate logistic regression model.

Presentation
Abstract was presented at the 10th International Conference on HIV Treatment and Prevention Adherence, 28th June 2015, Eden Roc Hotel, Miami Beach, Florida, United States of America.

Author Contributions
E.M.B was involved in the concept, design and acquisition of data. N.E.U and A.N.G. drafted the article and revised it critically for important intellectual content. I.B.O and E.M. were involved in the analysis and interpretation of data. All authors were involved in reviewing the final approval of the version to be published.

Source of Funding
The authors funded the study.

Conflict of Interest
The authors declare no conflict of interest.

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Citation: Bisong E, Udonwa N, Gyuse A, Okokon I, Monjok E. Clinical correlates of diarrhea and gut parasites among human immunodeficiency virus seropositive patients. Recent Adv Biol Med. 2017; 3:110-117.