

## Parasitic diarrhoea in treatment-naïve HIV-positive patients attending the University of Ilorin Teaching Hospital (UIH) Highly Active Antiretroviral Treatment (HAART) Clinic

Joseph A.A<sup>1\*</sup>, Ano-Edward G.H<sup>2</sup>

<sup>1</sup>Department of Medical Microbiology and Parasitology, College of Health Sciences, Bowen University Iwo, Osun State, Nigeria. <sup>2</sup>Department of Anatomic Pathology, College of health sciences, Bowen University, Iwo, Osun State, Nigeria.

\*Corresponding author: adejokejoseph2012@gmail.com

Received: 16.05.16; Accepted: 03.11.16; Published: 09.11.16

### ABSTRACT

**Background:** HIV is a public health issue with diarrhoea being the commonest gastrointestinal symptom especially in individuals with lower CD4+ cell counts. Most times, parasitic infections present as diarrhoea. Depending on geographical location, the pathogens responsible for diarrhoea vary. **Aim:** To relate the degree of immunodeficiency in HIV-infected patients to diarrhoea as a result of infestation by parasitic agent. **Methods:** 250 HIV positive and 250 HIV negative participants were recruited. Stool and blood samples were taken from all participants. Macroscopic and microscopic examinations of the stool were done while CD4+ count was estimated from the blood sample collected. Wet preparation of stool sample was done and concentrated stool was used for modified Ziehl Neelsen staining. **Results:** Diarrhoea was present in 200 participants, 118 of which were among the HIV positive group. Parasites were demonstrated in 82.3% of the test participants with diarrhoea and 17.7% of the controls with diarrhoea. Of the HIV positive with diarrhoea, 70.3% had a CD4 <200 cells/ $\mu$ l and 29.7% had a CD4 of 200-500cells/ $\mu$ l. Parasites in both groups were *Ascaris lumbricoides*, *Balantidium coli*, *Entamoeba histolytica*, *Schistosoma mansoni*, Hookworm, *Strongyloides stercoralis* and coccidian parasites though at varying frequencies. Of the 79 with parasites, 60 had single parasitosis, while 19 had multiple parasitosis. CD4 count was the only variable that correctly predicts presence of diarrhoea. **Conclusion:** Diarrhoea associated with parasitic infection HIV patients is a function of the immune status of the individual.

**Key words:** People Living with HIV/AIDS (PLWHA), HIV/AIDS, diarrhoea, intestinal parasite, HAART NAÏVE, immunosuppression

### INTRODUCTION

HIV is a global public health issue and a serious health and development challenge.<sup>[1]</sup> "Since 2000, 38.1 million people have become infected with HIV and 25.3 million people have died of AIDS-related illnesses".<sup>[2]</sup> Currently,

about 34 million people live with HIV.<sup>[1]</sup> About 25.8 million cases are in sub-Saharan Africa, accounting for 70% of the global total.<sup>[2]</sup> Only 54% of all People Living With HIV/AIDS (PLWHA) know that they are infected with the virus.<sup>[3]</sup>



Primarily, HIV affects people in their most productive period, and 50% of new infections are among those less than 25 years.<sup>[4]</sup> Many of the countries that are hardest hit by HIV also suffered from other infectious diseases. A major health problem among HIV seropositive patients is superimposed infection due to the defect of immunity. The primary site of disease in HIV infection remains the gastrointestinal (GI) tract.<sup>[5]</sup> About 50% of HIV-infected patients have GI symptoms, and most of them develop GI complications.<sup>[6]</sup> Diarrhoea is the commonest GI symptom in HIV-positive patients.<sup>[7]</sup> The prevalence of diarrhoea among outpatients has been reported to range from 0.9 to 14%.<sup>[8,9]</sup> The prevalence of HIV has been shown to be more among homosexual men and individuals with lower CD4+ cell counts.<sup>[10]</sup> This is likely because it has been reported that risk of transmitting HIV from anal intercourse is significantly higher than vaginal. The rate ranges from 0.04 to 0.38% per act for female-to-male transmission in low and high income countries respectively, 0.08 to 0.30% per act for male to female transmission in low and high income countries, compared to 1.4 to 1.7% per act in anal transmission.<sup>[11,12]</sup> The pathogenesis of HIV/AIDS is associated with decline in T-lymphocytes, which has CD4 receptors.<sup>[13,14]</sup> "The end point therefore is the subsequent depletion of CD4+ T lymphocytes leading to a failure of both the cellular and the humoral aspects of the body's immunity with significant morbidity and mortality, as seen through the natural course of the disease".<sup>[15]</sup>

In hospitalized individuals with advanced HIV infection, up to 50% have diarrhea.<sup>[8]</sup> There is however significant geographic variation in the prevalence of diarrhoea and the spectrum of enteric pathogens.<sup>[16]</sup> Pathogens were identified in more than 50% of patients with advanced HIV and diarrhea.<sup>[17,18]</sup> In several studies, co-infections were common, emphasizing the importance of ruling out all pathogens thoroughly when evaluating diarrhoea.<sup>[19]</sup> Studies have demonstrated a varying clinical spectrum of diarrhoea, with pathogen-negative diarrhoea now representing the majority of patients.<sup>[20,21]</sup> Other studies have reported a dramatic decrease in cryptosporidial diarrhoea over the past 5 years.<sup>[8]</sup>

Literature search indicate that parasitic infections often manifest as diarrhoea and that significant disease have been recorded in 50–96% of cases with 90% prevalence rate reported in Africa.<sup>[22]</sup> Various species of protozoa have been implicated in acute and

chronic diarrhoea in HIV/AIDS; namely *Cryptosporidium parvum*, *Isospora belli*, *Microsporidium* species, *Entamoeba histolytica/Entamoeba dispar*, *Giardia intestinalis*.<sup>[23]</sup> Intestinal parasites are endemic in many regions of the world where HIV/AIDS is also prevalent.<sup>[24]</sup> Sub-Saharan Africa where Nigeria is located is among the regions where intestinal parasitic infections is entrenched and the largest burden of AIDS cases exist.<sup>[25]</sup>

It has been reported that infective causes of chronic diarrhoea can be easily diagnosed with satisfactory response to treatment except cryptosporidiosis and HIV-related enteropathy.<sup>[26]</sup> To ensure adequate management guidelines for HIV/AIDS, its prevalence by laboratory diagnostic measures are required since there is a geographical variation in the pathogens responsible diarrhoea in HIV/AIDS patients.<sup>[22]</sup>

Medications such as protease inhibitors, including nelfinavir and saquinavir, are common cause of diarrhoea in the early stage of HIV. This form of diarrhoea is usually self-limiting, lasting less than 2 to 4 weeks. However, chronic diarrhoea may be seen even in patients with improved CD4 cell count and decreased viral load.<sup>[27]</sup> Other aetiologies of diarrhoea include idiopathic colitis, enteropathogenic *Escherichia coli*, and small bowel bacterial overgrowth.<sup>[27]</sup> Some studies have suggested that HIV may be a diarrhoeal pathogen since viral proteins are found in the gut and the virus has been identified in histologic specimens from the GI tract tissue in about 40% of patients; confined to lamina propria macrophages and enterochromaffin cells.<sup>[8]</sup> "Intestinal HIV infection may also affect local humoral immunity and cause motility disturbances via effects on autonomic nerves".<sup>[15,28,29,30]</sup>

"An 'idiopathic AIDS enteropathy' has been proposed to account for the diarrhoea in HIV-infected patients who lack an identifiable pathogen".<sup>[8]</sup> This is probably due to the indirect effects of HIV on enteric homeostasis.<sup>[8]</sup> Though the manifestations is still controversial, the term denotes a chronic diarrhoeal illness with no identified aetiology in patients with advanced HIV disease.<sup>[8]</sup> Some reports suggest the inclusion of mucosal hypoproliferation as a defining feature while others reported that enteric HIV infection may cause mucosal atrophy, which impairs absorption in the small intestine with consequent diarrhoea and weight loss.<sup>[8]</sup>

About 9% of PLWHA live in Nigeria.<sup>[2]</sup> Though HIV prevalence among Nigerian adults is significantly low (3.2%) when compared with other sub-Saharan African countries such as South Africa (19.1%) and Zambia (12.5%),<sup>[31]</sup> about 3.2 million people were reported to have HIV in 2013 in Nigeria.<sup>[32]</sup> "Nigeria, together with South Africa and Uganda, account for almost 50% of all annual new HIV infections in sub-Saharan Africa".<sup>[33,34]</sup> In addition, about 210,000 people died of AIDS-related illnesses in Nigeria in 2013, which is about 14% of the world total.<sup>[34]</sup> The major cause of morbidity and mortality in the HIV infected, and also the most prevalent symptom patient present with is diarrhoea. Since there is a geographic variation in the prevalence of diarrhoea and the spectrum of enteric pathogens implicated, the need to evaluate extensively the prevalence and the likely pathogens that causes of this symptom in this population, in this geographical location is pertinent.

The study is aimed at examining the relationship between the degree of immunodeficiency in HIV infected patients using CD4 count and diarrhoea as a result of infestation by parasitic agent.

## METHODOLOGY

The University of Ilorin Teaching Hospital where the study was carried out serves as a referral hospital to surrounding states including Niger, Kogi, Oyo, Ekiti, Ondo and Osun states. The hospital runs a Highly Active Antiretroviral Therapy (HAART) clinic supported previously by the Institute Of Human Virology, Nigeria (IHVN), but now supported by Management Science for Health (MSH) as at the time of this study. The clinic was established on September 3rd, 2008 and the total number of enrollee as at time of study was 5433 made up of 1885 adult males, 2874 adult females, 329 paediatric males and 345 paediatric female patients. Of the adult enrollees, 1498 have been commenced on antiretroviral drug.<sup>[35]</sup>

Sample size when studying proportions with population less than ten thousand (10,000) can be calculated using the formula below:<sup>[36]</sup>

$$nf = \frac{n}{1 + n/N}$$

where  $n_f$  - the desired sample size when population is less than 10,000

$n$  - the desired sample size when the population is more than 10,000

$N$  - the estimate of the population size. it is total adult population minus population on drugs.

$$N = (2874 + 1885) - 1498 = 3261$$

$n$  can be calculated using the formula

$$n = Z^2 pq / d^2$$

where  $n$  = desired sample size when population is greater than 10,000

$z$  = standard normal deviate, usually set at 1.96, which corresponds to the 95<sup>th</sup> confidence level

$p$  = proportion in the target population estimated to have a particular characteristic. Previous studies done at this centre reported a prevalence rate of 87.8% for intestinal parasitosis among adult HIV seropositive patients.<sup>[19]</sup>  $P$  therefore was set at 0.878.

$$q = 1.0 - p$$

$d$  = degree of accuracy desired, usually set at 0.05

$$q \text{ therefore will be } 1 - 0.878 = 0.122.$$

Based on these formulae, sample size for the study was estimated thus:

$$n = (1.96)^2 * 0.878 * 0.122 / 0.05^2$$

$$= 164.6$$

$$\sim 165$$

$$nf = \frac{n}{1 + n/N}$$

$$\text{If } n = 165,$$

$$nf = \frac{165}{1 + 165/3261}$$

$$= 157.14$$

$$\sim 157$$

Two hundred and fifty test subjects were however recruited for the study in order to improve the statistical power of the study findings.

Purposive sampling was done to select participants into the study, selecting consecutive patients presenting to the HAART clinic for enrolment into care. Included in the study were HIV positive individuals yet to commence ART while HIV seropositive patients who have been commenced on HAART and those who have being on antimicrobials in the last two (2) weeks prior to sample collection were excluded from the study. Equal number of apparently healthy age and sex matched patients who were HIV seronegative and attending the General Outpatient Clinic of the hospital were recruited as control. Stool and venous blood samples were collected from every participant and sent to the Medical Microbiology and Parasitology department research laboratory. Macroscopic and microscopic examinations of the stool samples were done while CD4+ count was estimated from the blood sample collected. An interviewer-administered questionnaire was

also completed at recruitment for all participants.

Ethical clearance was sought and obtained from the Ethical and research committee of UITH and a written informed consent was also obtained from the participants after carefully explaining the concept of the study to them. Permission was equally obtained from the Management Science for Health, Nigeria via the officer in charge of the UITH HAART clinic, being the representative of the institute in the hospital.

#### **Stool concentration**

Faecal suspension was sieved through a disposable paper funnel into a 15 ml conical centrifuge tube. 0.85% saline was added through the debris on the gauze to bring the volume in the centrifuge tube to 15 ml. Suspension was centrifuged at 500 × g for 10 minutes, supernatant decanted and 10 ml of 10% formalin added to the sediment and mixed thoroughly with wooden applicator sticks. 4 ml of ethyl acetate added and suspension centrifuged at 500 × g for 10 minutes. The top layers of supernatant were decanted and with the use of a cotton-tipped applicator, debris from sides of the centrifuge tube was removed. Several drops of 10% formalin to re-suspend the concentrated specimen was added.<sup>[37]</sup>

#### **Stool wet preparation**

A small amount of the stool specimen was placed on a microscope slide and a drop or two of saline was added to the specimen and mixed. A cover slip was placed on mixture and examined under the light microscope at 40x magnification.<sup>[38]</sup>

#### **Modified Ziehl Neelsen stain**

Faecal smears is made from the concentration deposit, allowed to air dry, fixed in methanol for 3 minutes, stained with strong carbol fuchsin for 15-20 minutes and rinse thoroughly in tap water. Decolourisation in acid alcohol (1% HCl in methanol) for 15-20 seconds was done, rinsed thoroughly in tap water, counterstained with methylene blue for 30-60 seconds and rinsed thoroughly and air dry. Examination using x40 and x100 objectives using light microscopy.<sup>[39]</sup>

#### **CD4+ count estimation**

The CD4 + cell count was performed using the CyFlow® SL (PARTEC, Berlin, Germany) counter, a portable desktop flow cytometer which uses fluorescent-labelled anti CD4+ monoclonal antibodies to capture CD4+ cells

from whole blood and allows automated counting.<sup>[40]</sup>

#### **Statistical analysis**

Clinical findings and laboratory results were recorded in the study questionnaire and analyzed using the Statistical Package for Social Sciences (SPSS), version 19. Results were presented in tabular forms and figures as found applicable. Categorical variables were compared by Chi square test and continuous variables were described by means ± SD and compared by the Student's T-test. Statistical significance was tested at predetermined *p*-value of <0.05. Other statistical tests used were Spearman Correlation, a non-parametric test that measures the strength of association between two ranked variables. Results are presented in tabular forms and figures as found applicable.

## **RESULTS**

Diarrhoea was present in 200 out of the sampled 500 participants, 118 of which were among the HIV positive test group and the remaining 82 were among the HIV negative control group (table 1). Presence of parasite(s) was demonstrated in 79(82.3%) of the test participants with diarrhoea and 17(17.7%) of the control participants who presented with diarrhoea (table 1). Of the 118 HIV positive with diarrhoea, 83(70.3%) had a CD4 of <200 cells/μl and 35(29.7%) had a CD4 of 200-500cells/μl.

The identified ova of parasites in both groups at varying frequencies, were *Ascaris lumbricoides*, *Balantidium coli*, *Entamoeba histolytica*, *Schistosoma mansoni*, Hookworm, *Strongyloides stercoralis* and oocyst of the coccidian parasites (table 2). Of the 79 with parasite, 60 had a single species of parasite (single parasitosis), while the remaining 19 had more than one species of parasite present (multiple parasitosis) (table 3). Likely causes of diarrhoea were examined and majority of the participants (173 test; 216 of control) source their water from borehole, 63 of test and 108 of control from tap water, 50 of test and 85 of control from well water, while 14 of test and 18 of control source from stream. Concerning their hygienic practices, 174 of the test and 231 of the control wash fruits before eating, 194 of the test and 239 of the control wash hands after defecating, and 187 of the test and 243 of the control had modern toilet facilities in their homes (figure 1).

Table 1: Prevalence of diarrhoea and intestinal parasitosis

	HIV POSITIVE N (%)	HIV NEGATIVE N (%)	$\chi^2$	p-VALUE
Diarrhoea (n = 500)				
Yes	118 (47.2)	82 (32.8)		
No	132 (52.8)	168 (67.2)	10.8	0.001
Patients with Diarrhoea (n = 200)				
Parasite present	79 (82.3)	17 (17.7)		
Parasite absent	39 (37.5)	65 (62.5)	41.4	0.001
Patients without diarrhoea (n = 300)				
Parasite present	73 (57.5)	54 (42.5)		
Parasite absent	59 (34.1)	114 (65.9)	56.8	0.001

Table 2: Prevalence of intestinal parasitosis in HIV positives

PARASITE	SUBJECT N (%)	CONTROL N (%)	$\chi^2$	p-VALUE
<i>Ascarislumbricoides</i>	26 (10.4)	15 (6.0)	2.951	0.086
<i>Balatidium coli</i>	0 (0.0)	1 (0.4)	0.000	1.000 <sup>Y</sup>
<i>Entamoebahistolytica</i>	0 (0.0)	1 (0.4)	0.000	1.000 <sup>Y</sup>
<i>Fasciolabuski</i>	0 (0.0)	1 (0.4)	0.000	1.000 <sup>Y</sup>
Hook worm	9 (3.6)	6 (2.4)	0.600	0.439
<i>Schistosomamansonii</i>	0 (0.0)	1 (0.4)	0.000	1.000 <sup>Y</sup>
<i>Strongyloidesstercoralis</i>	5 (2.0)	0 (0.0)	3.200	0.074 <sup>Y</sup>
Coccidian	139 (55.6)	17 (6.8)	95.410	0.001*
<i>Cryptosporidium</i>	84 (33.6)	11 (4.4)	56.095	<0.001*
<i>Cyclospora</i>	52 (20.8)	5 (2.0)	38.754	<0.001*
<i>Isospora</i>	3 (1.2)	1 (0.4)	0.250	0.617 <sup>Y</sup>
No parasite	98 (39.2)	209 (83.6)	40.134	<0.001*

Multiple parasites present in some patients;  $\chi^2$ : Chi square; Y: Yates' chi square (when 20% of expected count is less than 5); \* P-value less than 0.05 (i.e. statistically significant)

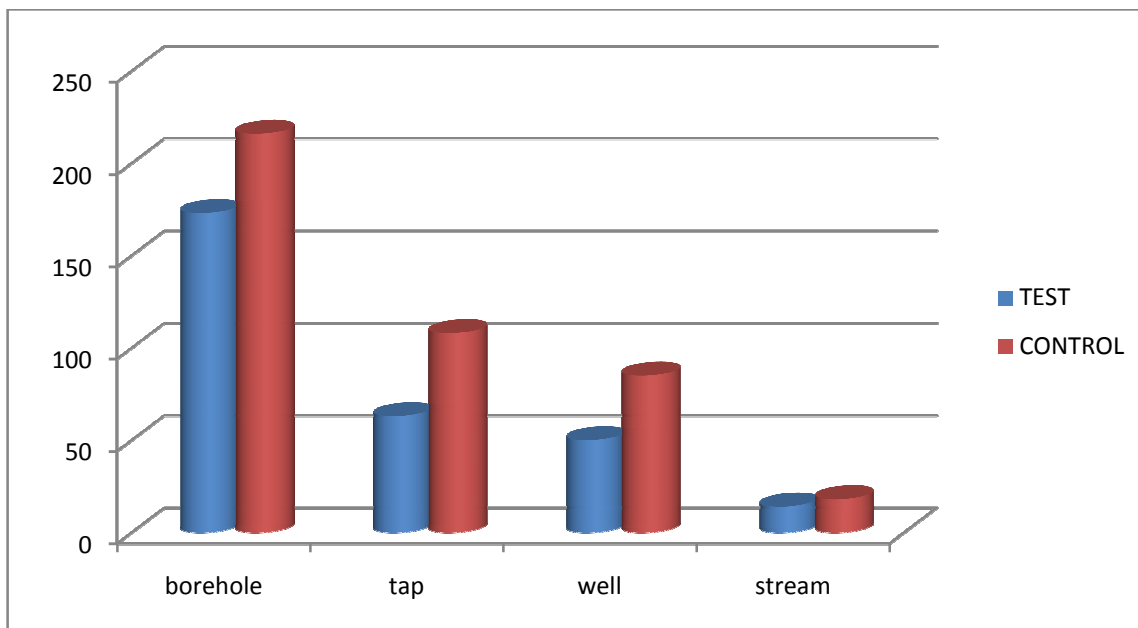


Figure 1: Source of water

Table 3: Relationship between parasite number and diarrhoea in HIV patients

Parasite number	Diarrhoea		Total	$\chi^2$	p-value
	Yes	No			
None	39 (33.1)	59 (44.7)	98 (39.2)	5.481	0.065
Single	60 (50.8)	62 (47.0)	122 (48.8)		
Multiple	19 (16.1)	11 (8.3)	30 (12.0)		
Total	118 (100.0)	132 (100.0)	250 (100.0)		

Relating hygiene practices and source of water in respondents to the likelihood of presenting with diarrhoea, it was noted that 46.6% had diarrhoea despite washing fruits and vegetables before eating, 49% had diarrhoea despite washing hands after defecating, and 46% had toilet facilities in their homes. Concerning their source of water, 71.4% of those with diarrhoea source their water from stream, 62% of them from well, 60.3% from tap borne water and 50.9% from borehole (tables 4 and 5).

A multivariate analysis was done using Forward Binary logistic regression in order to determine the predictors of diarrhoea in HIV patients. The model that best predicts presence of diarrhoea and its variables are shown in table 6. The model correctly predicts 71.0% cases of presence of diarrhea in the study participants. Variables excluded by the model were viral load, washing of fruits and

vegetables before eating, sources of water (stream, well, borehole and tap).

## DISCUSSION

Diarrhoea is a common presenting complaint in HIV-infected patients. The infectious aetiological agents include both opportunistic agents that consistently cause severe and chronic gastrointestinal disease and non-opportunistic agents that usually cause acute treatable diarrhoeal illness.<sup>[41]</sup> Gastrointestinal parasitic infection is common in the tropics. The prevalence of diarrhoea in HIV positives reported in this study is 47.2%. Similar to what was reported by Haileeyesus *et al.* in Ethiopia, HIV infection is a risk factor for *Cryptosporidium* and other intestinal parasites infections and diarrhoea.<sup>[42]</sup> Their study revealed a lower prevalence of diarrhoea-causing pathogens and *Cryptosporidium* in HIV patients on ART.<sup>[42]</sup>

Table 4: Relationship between hygiene practice, source of water and diarrhoea in HIV patients

Hygiene practices	Diarrhoea			$\chi^2$	p-value
	Yes	No	Total		
Wash fruit and vegetables before eating					
Yes	81 (46.6)	93 (53.4)	174 (100.0)	3.397	0.065
No	20 (64.5)	11 (35.5)	31 (100.0)		
Wash hands after defecating					
Yes	95 (49.0)	99 (51.0)	194 (100.0)	0.130	0.719
No	6 (54.5)	5 (45.5)	11 (100.0)		
Toilet facility available at home					
Yes	86 (46.0)	101 (54.0)	187 (100.0)	11.126	0.001*
No	15 (88.2)	2 (11.8)	17 (100.0)		
Source of water					
Stream					
Yes	10 (71.4)	4 (28.6)	14 (100.0)	2.638	0.104
No	90 (48.9)	94 (51.1)	184 (100.0)		
Well					
Yes	31 (62.0)	19 (30.8)	50 (100.0)	3.536	0.060
No	69 (46.6)	79 (53.4)	148 (100.0)		
Tap					
Yes	38 (60.3)	25 (39.7)	63 (100.0)	3.559	0.059
No	62 (45.9)	73 (54.1)	135 (100.0)		
Borehole					
Yes	88 (50.9)	85 (49.1)	173 (100.0)	0.072	0.789
No	12 (48.0)	13 (52.0)	25 (100.0)		

$\chi^2$ : Chi square; \*: P-value <0.05

Table 5: Relationship between hygiene practice, source of water and diarrhoea in control group

Hygiene practices	Diarrhoea		Total	$\chi^2$	p-value
	Yes	No			
Wash fruit and vegetables before eating					
Yes	77 (33.3)	154 (66.7)	231 (100.0)	0.392	0.531
No	5 (26.3)	14 (73.7)	19 (100.0)		
Wash hands after defecating					
Yes	77 (32.2)	162 (67.8)	239 (100.0)	1.631 <sup>Y</sup>	0.202
No	2 (100.0)	0 (0.0)	2 (100.0)		
Toilet facility available at home					
Yes	78 (32.1)	165 (67.9)	243 (100.0)	1.628 <sup>Y</sup>	0.202
No	3 (3.7)	1 (0.6)	4 (100.0)		
Source of water					
Stream					
Yes	6 (33.3)	12 (66.7)	18 (100.0)	0.003	0.960
No	75 (32.8)	154 (67.2)	229 (100.0)		
Well					
Yes	25 (29.4)	60 (70.6)	85 (100.0)	0.962	0.327
No	57 (35.6)	103 (64.4)	160 (100.0)		
Tap					
Yes	39 (36.1)	69 (63.9)	108 (100.0)	0.682	0.409
No	41 (31.1)	91 (68.9)	132 (100.0)		
Borehole					
Yes	73 (33.8)	143 (66.2)	216 (100.0)	0.009	0.924
No	8 (34.8)	15 (65.2)	23 (100.0)		

$\chi^2$ : Chi square; Y: Yates corrected chi square; \*: P-value <0.05

Table 6: Predictors of diarrhoea in HIV patients

Variables	B	p-value	OR	95% C.I	
				Lower	Upper
CD 4 count	-0.005	<0.001*	0.995	0.993	0.997
Washing of hands after defecating	-2.237	0.076	0.107	0.009	1.261
Presence of toilet facility	-3.225	0.005*	0.040	0.004	0.380

B: Coefficient of Binary logistic regression; OR: Odds ratio; C.I: Confidence Interval; \*: p value <0.05, R<sup>2</sup>: 0.254. Predictive value: 71.0%.  $\chi^2$ :40.728; p: <0.001

Variables excluded by the model: Viral load, Washing of fruits and vegetables before eating, Sources of water (Stream, Well, Borehole and Tap)

In this study, the prevalence of Coccidian parasitic infection in the HIV positive patients, is 55.6%, the highest and statistically significant compared with the other parasites (p= 0.001). This is similar to the report of Smith *et al.* in India where 38 out of the 113 HIV positive stool samples were found to have intestinal parasites present, 29 (76.3%) of which are coccidian parasites alone or with other parasites.<sup>[43]</sup> Coccidian parasite is an opportunistic infection common in HIV patients, though can cause self-limiting intestinal infection in immunocompetent hosts too. Infection in the immunocompromised is

more severe, probably because the immune system which reduces the formation of type 1 merozoites as well as the number of thin-walled oocysts which initiates an infection is deficient in the HIV infected.<sup>[44]</sup> Of the coccidian parasites detected, *Cryptosporidium* was detected in 33.6% of the HIV positive patients, *Cyclospora* in 20.8% and *Isospora* in 1.2% of them. Looking at the spectrum of parasites seen, there was no statistically significant difference between subjects and control when protozoa parasites are concerned (p>0.05) with the exception of the coccidian parasites whose prevalence was significantly different



between test and control ( $p=0.001$ ). This is in keeping with previous studies done at UITH Ilorin. The findings of Erhabor and Obunge in Niger Delta region of Nigeria is similar to this also, where they reported cryptosporidiosis to be significantly higher in the HIV positive with diarrhoea than their HIV negative counterpart.<sup>[45]</sup> Diarrhoea was common and most strongly associated in patients with CD4+ cell counts less than 200 (70.3%). In 33.1% of the patients with diarrhea there were no parasites identified while some of the diarrheal episodes were undiagnosed. This suggests that unidentified pathogens or primary HIV enteropathy are major causes of diarrhoea in the population.<sup>[46,47]</sup> In keeping with these findings is the report of Suresh *et al.* in Venezuela and Weber *et al.* in Swiss where intestinal infections were diagnosed in less than 50% of chronic diarrhoeal episodes.<sup>[46,47]</sup> In addition to not isolating any pathogen in the majority of the samples, wherever pathogens were found, protozoan infections dominated over the bacterial causes.<sup>[46,47]</sup> Needless to say that all aetiological agents cannot be easily diagnosed in Africa on routine basis because of limited diagnostic facilities and trained personnel coupled with the fact that diagnosis could require high tech instrument and molecular studies.<sup>[20]</sup>

There is a negative association between source of water and hygiene practices, and the presence of diarrhoea in HIV positive individuals and a rather strong positive association between CD4 levels and presence of diarrhoea. This is a pointer to the possibility that diarrhoea in the HIV positive is a function of their depressed immune status, more than their lifestyle practices. This is in deviant to what Suresh and Weber reported which is a strong negative association between diarrhoea and CD4 count.<sup>[46,47]</sup>

Progressive immunosuppression is associated with a rise in the prevalence of GI features. In HIV-infected patients in the groups CD4+ > 500 cells/ $\mu$ L, 200 cells/ $\mu$ L -500 cells/ $\mu$ L and in the AIDS patients CD4+ < 200 cells/ $\mu$ L, diarrhoea was 0, 29.7 and 70.3%. Diarrhoea was also found to be significantly present in HIV positives compared with HIV negative controls ( $p=0.001$ ); intestinal parasitosis was also significantly associated with HIV seropositivity irrespective of whether patient is diarrhoeic or not ( $p=0.001$ ). This is in agreement with findings in Kano where it was reported that diarrhoea is a frequent presenting complaint in HIV positives, especially at CD4+ count of <200cells/ $\mu$ L. This

finding is however not surprising for gastrointestinal disease, particularly diarrhoea, which is the commonest clinical presentation of HIV/AIDS in Africa and other developing countries, occurring in 90-100% of patients with HIV infection.<sup>[48]</sup> It has also been noted that due to down regulation of the immune system in the HIV infected, opportunistic infections, parasitic and non-parasitic, occur more commonly in the HIV infected.<sup>[49]</sup>

It was also observed that the presence of GI parasites predisposed to development of diarrhoea in HIV infected patients. The presence of single (one specie) or multiple (more than one species of parasite) parasitoses was found not to be statistically significant.

Several environmental and socioeconomic factors have been identified to predispose an individual to diarrhoea. They include poor sanitary conditions, unhygienic practices, absence of portable water, poor housing and poverty.<sup>[50,51,52]</sup> In this study however, these factors did not significantly influence the presence of diarrhoea in HIV positives compared to their HIV negative controls. CD4 count was the only variable seen to influence the development of diarrhoea. This is a pointer to the fact that the presence and persistence of gastrointestinal parasites in the HIV infected and the subsequent passage of watery stool that results is a function of the suppressed or deficient immune system of the host much more than the physical and socioeconomic status of the individual.

## CONCLUSION

Diarrhoea in HIV occurs irrespective of the geographical location of the individual, the socioeconomic status of the individual, the daily activities and lifestyle but rather it is a function of the immune status of the individual. The more immunosuppressed the individual is, the greater the likelihood of presenting with diarrhoea associated with parasitic infection. This might be due to marked reduction in both the peripheral and the GI CD4 cells quantity as well as due to alteration in structure and function of enterocytes caused by the pathogen (HIV).<sup>[53]</sup>

## RECOMMENDATION

1. Screening for parasitic infection should form part of the baseline investigations when enrolling clients into HIV

care program and the specific investigation should include stool for ova of parasite.

2. Antiparasitic agents should be included when treating treatment naïve HIV infected patients with diarrhoea.

3. Antiparasitic agents should be commenced prophylactically at CD4+ T cell count less than 200 cells/ $\mu$ l.

## REFERENCES

1. The Henry J. Kaiser Family Foundation: The Global HIV/AIDS Epidemic. UNAIDS. Fact Sheet: The Global AIDS Epidemic; 2012; 1:1-3. Available at <http://kff.org/global-healthpolicy/factsheet/theglobalhivaids-epidemic>. Assessed 05.03.13.
2. UNAIDS Fact Sheet 2014 statistics.
3. UNAIDS 2015. How AIDS changed everything.
4. UNAIDS. Epidemiological Core Slides- GAP report: Global Summary of the AIDS Epidemic; 2012.
5. Veazey RS, DeMaria M, Chalifoux LV, Shvetz DE, Pauley DR, Knight HL, Rosenzweig M, Johnson RP, Desrosiers RC, Lackner AA. Gastrointestinal tract as a major site of CD4+ T cell depletion and viral replication in SIV infection. *Science* 1998;280:427-31.
6. Bhajjee F, Subramony C, Tang S-J, Pepper DJ. Human Immunodeficiency Virus-Associated Gastrointestinal Disease: Common Endoscopic Biopsy Diagnoses. *Pathology Research International* 2011;2011:247923.
7. Kristeen C. HIV and Diarrhea: Causes, Treatments, and more. Available at <http://www.healthline.com/health/hiv-aids/diarrhoea>. Assessed on 25<sup>th</sup> July, 2016.
8. Johannes K, Lawrence S, Scott F. Gastrointestinal Manifestations of HIV. HIV In Site Knowledge Base Chapter. University of California. June 1998. <http://hivinsite.ucsf.edu/InSite?page=kb-04-01-11>.
9. Wilcox C, Rabeneck L, Friedman S. AGA Technical Review: Malnutrition and cachexia, chronic diarrhea, and hepatobiliary disease in patients with human immunodeficiency virus infection. *Gastroenterology* 1996;111:1724-1752.
10. Pathogenesis of HIV/AIDS. Available at <http://www.niaid.nih.gov/topics/hivaids/understanding/howhivcausesaids/pages/relationshiphivaids.aspx>. accessed on 10/09/16.
11. HIV/AIDS. Available at <https://www.en.wikipedia.org/wiki/HIV/AIDS>. accessed on 13/09/16
12. Beyrer C, Baral SD, van Griensven F, Goodreau SM, Chariyalertsak S, Wirtz AL, Brookmeyer R. Global epidemiology of HIV infection in men who have sex with men. *Lancet* 2012;380:367-77.
13. Luc K. The immune system and HIV:How HIV damages the immune system. Available at [http://www.itg.be/internet/e-learning/written\\_lecture\\_eng/ref\\_virology\\_and\\_immunology.pdf](http://www.itg.be/internet/e-learning/written_lecture_eng/ref_virology_and_immunology.pdf) assessed on 13/09/16.
14. Jonathan W. The pathogenesis of HIV-1 infection. *British Medical Bulletin* 2001;58:61-72. <http://bmb.oxfordjournals.org/content/58/1/61.full.pdf>. accessed on 13/09/16.
15. Awadh R.A. Gastrointestinal opportunistic infections in Human Immunodeficiency Virus Disease. *Saudi J Gastroenterol* 2009;15:95-99.
16. Vyas N, Pathan N, Aziz A. Enteric pathogens in HIV-positive patients with diarrhoea and their correlation with CD4+ T-lymphocyte counts. *Trop Parasitol* 2012;2:29-34.
17. Connolly GM, Shanson D, Hawkins DA, Webster JN, Gazzard BG. Non-cryptosporidial diarrhoea in human immunodeficiency virus (HIV) infected patients. *Gut* 1989;30:195-200.
18. Laughon BE, Druckman DA, Vernon A, Quinn TC, Polk BF, Modlin JF, Yolken RH, Bartlett JG. Prevalence of enteric pathogens in homosexual men with and without acquired immunodeficiency syndrome. *Gastroenterology* 1988;94:984-93.
19. Gastrointestinal manifestations in AIDS. Available at <http://www.icm.tn.gov.in/article/GASTROINTE-STINAL.htm>. Accessed on 3<sup>rd</sup> June, 2016
20. Wilcox CM, Schwartz DA, Cotsonis G, Thompson SE. Chronic unexplained diarrhea in human immunodeficiency virus infection: determination of the best diagnostic approach. *Gastroenterology* 1996;110:30-7.
21. Kearney DJ, Steuerwald M, Koch J, Cello JP. A prospective study of endoscopy in HIV-associated diarrhea. *Am J Gastroenterol* 1999;94:596-602.
22. Oguntibeju O.O. Prevalence of intestinal parasites in HIV-positive/AIDS patients in South Africa. *Malaysian Journal of Medical Sciences* 2006;13:68-73.
23. Sachin D, Ruchi K, Santosh S, Siddiqui AU. The prevalence of intestinal parasitic infections in HIV infected patients in a

- rural tertiary carehospital of Western Maharashtra. (A 5 year study). *Journal of Clinical and Diagnostic Research* 2011;5:210-212.
24. Shimelis A, Berhanu E, Girmay M, Zelalem Aand Techalew S. Intestinal parasitic infections in relation to HIV/AIDS status, diarrhea and CD4 T-cell count. *BMC Infectious Disease* 2009; 9:155.
25. UNAIDS/WHO, AIDS epidemic update 2006. Available at [http://www.un-ngls.org/spip.php?page=article\\_s&id\\_article=186](http://www.un-ngls.org/spip.php?page=article_s&id_article=186). Assessed on 29th February, 2016.
26. Smith PD, Lane HL, Gill VG, Manilchewwitz JF, Quinnan GV, Fauci AS. Intestinal infections in patients with AIDS: Aetiology and response to therapy. *Ann Intern Med* 1988;108:328–333.
27. Steuerwald MH, Leib S, Tauber M. Small bowel bacterial overgrowth: A cause of diarrhea in patients with AIDS? *Gastroenterology* 1997;112:Abs 1097A.
28. Kotler DP, Scholes JV, Tierney AR. Intestinal plasma cell alterations in acquired immunodeficiency syndrome. *Dig Dis Sci* 1987;32:129-38.
29. Mathan MM, Griffin GE, Miller A, Batman P, Forster S, Pinching A, Harris W. Ultrastructure of the jejunal mucosa in human immunodeficiency virus infection. *J Pathol* 1990;161:119-27.
30. Griffin GE, Miller A, Batman P, Forster SM, Pinching AJ, Harris JR, Mathan MM. Damage to jejunal intrinsic autonomic nerves in HIV infection. *AIDS* 1988;2:379-82.
31. HIV and AIDS in Zambia. UNAIDS. Gap Report.2012. [www.avert.org/node/408](http://www.avert.org/node/408)
32. UNAIDS.Epidemiology Fact Sheet on HIV and AIDS in Nigeria, 2014. accessed 01 June, 2016.
33. HIV and AIDS in Nigeria. <http://www.avert.org/professionals/hiv-around-world/sub-saharan-africa/nigeria>
34. UNAIDS. The gap report. 2014.
35. IHVN UITH HAART clinic record. Accessed on 19.02.12.
36. Araoye M. Research Methodology and Biostatistics for students and health sciences. Nathadex publishers.1st edition, 2003; 6: 115-123.
37. Global Health - Division of Parasitic Diseases and Malaria. Diagnostic Procedures. Formalin-Ethyl Acetate Sedimentation Concentration available at <http://www.cdc.gov/dpdx/diagnosticProcedures/stool/specimenproc.html>
38. Global Health - Division of Parasitic Diseases and Malaria. Diagnostic Procedures. DPDx - Laboratory Identification of Parasitic Diseases of Public Health Concern. Available at <http://www.cdc.gov/dpdx/diagnosticProcedures/stool/microexam.html>
39. UK Neqas. Modified Ziehl Neelsen. [http://ukneqasmicro.org.uk/parasitology/images/pdf/FaecalParasitology/DiagnosticTests/Modified\\_Ziehl.pdf](http://ukneqasmicro.org.uk/parasitology/images/pdf/FaecalParasitology/DiagnosticTests/Modified_Ziehl.pdf).
40. Sysmex Partec. Cyflow@SLcounter. Operation manual. Available at [www.sysmex-partec.com/instrumentation/products/cyflow\\_sl\\_microbiology.html](http://www.sysmex-partec.com/instrumentation/products/cyflow_sl_microbiology.html)
41. Smith PD, Lane HL, GillVG, Manilchewwitz JF, QuinnanGV, Fauci AS et al. Intestinal infections in patients with AIDS:Etiology and response to therapy. *Ann Intern Med* 1988;108:328-33.
42. Haileeyesus A, TekluW, and Beyene P. High prevalence of diarrhoeagenic intestinal parasite infections among Non-ART HIV patients in Fitcha Hospital, Ethiopia. *PLoS One* 2013;8:e72634.
43. Gupta S., Narang S., Nunavath V., Singh S. Chronic diarrhoea in HIV patients:prevalence of coccidian parasites. *Indian Journal of Medical Microbiology* 2008;26:172-5.
44. White A. Cryptosporidiosis. Available at <https://en.wikipedia.org/wiki/Cryptosporidiosis#Pathogenesis>. Accessed 2<sup>nd</sup> June, 2016.
45. Erhabor O, Obunge O, Awah I. Cryptosporidiosis among HIV-infected persons in the Niger Delta of Nigeria. *Niger J Med*2011;20:372-5.
46. Gabriela C, Alejandro A, Leonor P, Giuseppe F, Julio C, Andreina B and Luz N. Isosporiasis in Venezuelan adults infected with Human Immunodeficiency Virus: clinical characterization. *Am J Trop Med Hyg* 2003;69:217-222.
47. Weber R1, Ledergerber B, Zbinden R, Altwegg M, Pfyffer GE, Spycher MA, Briner J, Kaiser L, Opravil M, Meyenberger C, Flepp M. Enteric infections and diarrhea in human immunodeficiency virus-infected persons: prospective community-based cohort study. *Swiss HIV Cohort Study. Arch Intern Med* 2012;159:1473-80.
48. Wilcox CM. Etiology and evaluation of diarrhea in AIDS: A global perspective at the millennium. *World Journal of Gastroenterology* 2000;6:177-186.

49. Judie BA, Blake BT, Keith R.F. Mechanism of CD4+T lymphocyte cell death in HIV infection and AIDS. *J Gen Virol* 2003;84:1649-1661.
50. Edungbola D, Obi A. A review of human intestinal parasites in Nigeria; challenges and prospects for integrated control. *Nigerian Journal of Parasitology* 1992;13:27-37.
51. WHO. Action for the control of soil transmitted helminthiasis in Nigeria. Proceeding of an International workshop on strategies for the control of soil transmitted helminthiasis in Nigeria. Ile-Ife, Nigeria 7th- 9th May, 1991.
52. Nwoke B. The impact of changing human environment and climate change on emerging and re-emerging parasitic diseases. 28th Annual Conference of Nigerian Society for Parasitology, Owerri; Nigeria. 1-37.
53. Sain SL. Pathophysiology of HIV-associated diarrhoea. *Gastroenterology Clinics of North America* 1997;26:175-189.

**doi:** <http://dx.doi.org/10.14194/ijmbr.5.3.5>

**How to cite this article:** Joseph A.A, Ano-Edward G.H. Parasitic diarrhoea in treatment-naïve HIV-positive patients attending the University of Ilorin Teaching Hospital (UIH) Highly Active Antiretroviral Treatment (HAART) Clinic. *Int J Med Biomed Res* 2016;5(3):135-146

**Submit your valuable manuscripts to Michael Joanna Publications for:**

- User-friendly online submission
- Rigorous, constructive and unbiased peer-review
- No space constraints or colour figure charges
- Immediate publication on acceptance
- Unlimited readership
- Inclusion in AJOL, CAS, DOAJ, and Google Scholar

**Submit your manuscript at**  
[www.michaeljoanna.com/journals.php](http://www.michaeljoanna.com/journals.php)



## Submit your next manuscript to any of our journals that is the best fit for your research



### International Journal of Medicine and Biomedical Research

**Scope:** *IJMBR publishes cutting edge studies in medical sciences*

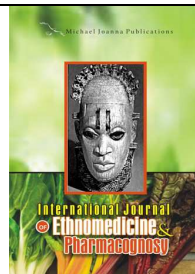
**Editor-in-Chief:** *Sofola A. Olusoga, MBBS, PhD, FAS*

**Deputy Editor:** *Lehr J. Eric, MD, PhD, FRCSC*

**URL:** [www.ijmbr.com](http://www.ijmbr.com)

**E-mail:** [editor@ijmbr.com](mailto:editor@ijmbr.com)

**Pissn:** 2277-0941, **eISSN:** 2315-5019



### International Journal of Ethnomedicine and Pharmacognosy

**Scope:** *IJEP publishes novel findings on the use of complementary and alternative medicine in the management of diseases*

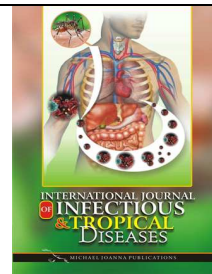
**Editor-in-Chief:** *Dickson A. Rita, B.Pharm, GCAP, PhD, MPSGh, MCPA*

**Deputy Editor:** *Kuete V., PhD*

**URL:** [www.ijepharm.com](http://www.ijepharm.com)

**E-mail:** [editor@ijepharm.com](mailto:editor@ijepharm.com)

**Pissn:** 2437-1262, **eISSN:** 2437-1254



### International Journal of Infectious and Tropical Diseases

**Scope:** *IJITD publishes interesting findings on infectious and tropical diseases of public health importance*

**Editor-in-Chief:** *Yang Z., PhD*

**Deputy Editor:** *Liping L.P., MD, PhD*

**URL:** [www.ijitd.com](http://www.ijitd.com)

**E-mail:** [editor@ijitd.com](mailto:editor@ijitd.com)

**Pissn:** 2384-6607, **eISSN:** 2384-6585

### Reasons to publish your manuscript with Michael Joanna Publications:

• User-friendly online submission • Rigorous, constructive and unbiased peer-review • No space constraints or coloured figure charges • Immediate publication on acceptance • Authors retain copyright • Inclusion in AJOL, CAS, CNKI, DOAJ, EBSCO, Google Scholar, and J-Gate • Unlimited and wide readership • Member of COPE and CrossRef

#### Editorial Director

Professor Sofola A. Olusoga,  
Department of Physiology,  
University of Lagos,  
Nigeria.

Tel: +234(0) 7093848134

Email: [enquiry@michaeljoanna.com](mailto:enquiry@michaeljoanna.com)

[www.michaeljoanna.com](http://www.michaeljoanna.com)

