

Peculiarities of Chronic Diarrhea in Enugu, Southeastern Nigeria

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Adult patients admitted with chronic diarrhea to the various wards of the University of Nigeria Teaching Hospital, Enugu, from August 1996 to October 1997 were evaluated further by detailed history-taking, thorough physical examination, serological testing for HIV infection, and stool microscopy. Of 189 patients with chronic diarrhea seen during the study period, 161 had human immunodeficiency virus (HIV) infection (85.2%) whereas 28 were HIV negative (14.9%). Other clinical findings such as weight loss, persistent cough, skin rash prolonged fever, genital ulcers, sore throat, chronic ear discharge, chronic vaginal discharge, oral thrush, herpes zoster, and sinusitis were significantly more frequent in the HIV-infected group. Diarrhea was equally more severe in this group than in the HIV-negative controls. Only *Entamoeba histolytica* (*E. histolytica*) was significantly more frequently identified in the HIV-infected patients compared with the HIV-negative group. However, since the *E. histolytica* was present mainly in its cyst form, it cannot be said to have any pathogenic role in the diarrhea. No acid-fast organism was identified. The microbial causes of chronic diarrhea in HIV-infected patients in Enugu may be significantly different from those reported in other parts of Africa and the developed world.

INTRODUCTION

Diarrheal diseases constitute a major cause of morbidity and mortality worldwide. In clinical practice, diarrhea can be a presenting symptom of nu-

merous diseases including primary intestinal disease and systemic illnesses such as diabetes mellitus. The precise definition of diarrhea is elusive, given the considerable variation in normal bowel habits. An increase in stool mass, stool frequency or stool fluidity is perceived as diarrhea by most patients.¹⁾ Because of the difficulty in objectively evaluating some of these parameters WHO defines diarrhea as “liquid stools 3 or more times a day, continuously or episodically, for more than one month.”²⁾

Chronic diarrhea is not a new problem in Africa. Before the outbreak of acquired immunodeficiency syndrome (AIDS) the main causes of chronic diarrhea in Africa were intestinal tuberculosis, schistosomiasis, amoebiasis, giardiasis, chronic pancreatitis with malabsorption, and lactose intolerance.³⁾ With the emergence of human immunodeficiency virus (HIV) disease, there has been a remarkable change in the epidemiology of chronic diarrhea, with the latter now bearing a high positive predictive value for HIV infection.^{4,5)} Diarrhea is so common in African HIV-infected patients that AIDS was at one time described as mainly enteropathic.⁶⁾

This study was therefore designed to highlight some of the clinical and microbial peculiarities of chronic diarrhea in south eastern Nigeria in this era of the AIDS pandemic.

MATERIALS AND METHODS

Adult patients with chronic diarrhea admitted to various wards of the University of Nigeria Teaching Hospital Enugu, from August 1996 to October 1997 formed the study population. Exclusion criteria included use of laxatives, antacids, or bismuth salts in the 2 weeks before specimen collection as these agents are known to be lethal to trophozoites of protozoa.⁷⁾ Also excluded were patients who had undergone contrast X-ray studies of the gastrointestinal tract in the preceding 2 weeks and patients on specific antiprotozoal drugs or broad-spectrum antibiotics.

A detailed history was obtained and physical examination conducted for all patients. Each patient was scheduled to provide three different stool samples separated by at least 3 days. The stools were passed in previously washed and air-dried bed pans, without urinating into the pan. Part of the stool was transferred to a specimen bottle using a spatula. The specimen was moved to the parasitology laboratory

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and examined within 1 hr of passing the stool. Each sample was subjected to microscopy, saline wet mount, iodine wet mount, buffered methylene blue wet mount, and formol-ether concentration.⁸⁾ The modified Ziehl- Neelsen (ZN) staining procedure was also carried out on both unconcentrated and concentrated samples.⁹⁾

The wet mounts were repeated on the concentrated samples. All the slides were examined systematically using a standard microscope (N J 242458/133144). All the patients had their blood screened for HIV infection and those who were positive were subjected to confirmation using western blotting.

The results were analyzed using means as a measure of central tendency and standard deviation as a measure of dispersion. Means and proportions were compared between the HIV-infected and HIV-negative groups at a significance level of < 0.05 using Student's *t*-test.

RESULTS AND DISCUSSION

Seroprevalence of HIV Infection

A total of 189 patients (117 men and 72 women) whose ages ranged between 15 years and 59 years met the inclusion criteria (Table 1). One hundred and sixty-one patients had HIV infection (85.2%) whereas 28 patients (14.9%) were HIV negative.

The observed high prevalence of HIV infection in patients with chronic diarrhea may be explained by the fact that only patients admitted to the ward were recruited. Recent studies show that AIDS accounts for a significant proportion of hospital admissions in Nigeria,¹⁰⁾ and therefore any hospital-based study is bound to be affected by this prevailing trend. Those patients who had chronic diarrhea but were not so ill as to require hospital admission were excluded because of our initial experience at the commencement of the study. It was difficult to ensure prompt examination of their stools if they had to come from their homes to submit the samples.

Stool Collection

Each of the 189 patients with chronic diarrhea was scheduled to submit three different stool samples for examination. Of them, 130 patients (68.8%) submitted all three samples, 40 patients (21.2%) submitted two samples each, and 19 patients (10.1%) submitted only one sample each. Thus 489 stool samples (86.2%) in all were examined, instead of

Table 1. Age and Sex Distribution of HIV Infected and HIV Negative Patients with Chronic Diarrhea

Age (years)	Males	Female	Total
15–19	1 (1)	7 (1)	8 (2)
20–24	6 (2)	14	20 (2)
25–29	15 (3)	13 (3)	28 (6)
30–34	19 (1)	13 (1)	32 (2)
35–39	19 (1)	6 (2)	25 (3)
40–44	23 (3)	3	26 (3)
45–49	16 (3)	2 (4)	18 (7)
50–54	3	1 (1)	4 (1)
55–59	(1)	(1)	1 (2)
Total	102 (15)	59 (13)	161 (28)

Figures in parentheses represent HIV negative patients.

567 samples if every patient had submitted three samples.

A stool collection rate of 86.2% is considered satisfactory when viewed against the background of certain factors that militated against 100% stool collection such as high mortality in some patients within the first week of admission and discharge against medical advice in some cases.

Other Clinical Findings

Apart from chronic diarrhea that was common to all patients, weight loss, skin rash, genital ulcers, amenorrhea, oral thrush, persistent cough, dysphasia, hemoptysis, chronic vaginal discharge, chronic ear discharge, hepatomegaly, and splenomegaly occurred more frequently in the HIV infected group than in the HIV negative group (Table 2). The explanation for this observation may be derived from the greater likelihood of opportunistic infections in the HIV infected group.

Characteristics of Diarrhea

Sixty (60) HIV infected patients (32.3%) had more than six bowel movements per day while only 4 HIV negative patients (14.3%) had more than six bowel movements per day since onset. (Table 3). Continuous diarrhea was recorded in 25 HIV infected patients (15.2%) and 2 HIV negative patients (84.5%) and in 26 HIV negative ones (92.9%). Liquid stool without blood or mucus occurred in 120 HIV infected patients (74.5%) and in 15 HIV negative patients (53.6%). Semi liquid stools without blood or mucus occurred in 29 HIV infected patients (18.0%) and in 8 HIV negative ones (28.6%). Stool with blood or mucus was reported by 12 HIV infected patients (7.5%) and by 5 HIV negative pa-

Table 2. Other Clinical Features of Patients with Chronic Diarrhea

Clinical presentation	Chronic Diarrhea with HIV infection (n = 161)	Chronic diarrhea without HIV infection (n = 28)	p-Value
Loss of weight	82 (50.31)	8 (28.57)	< 0.05
Persistent cough	62 (38.57)	7 (25.00)	< 0.05
Skin rash	30 (18.63)	4 (14.28)	< 0.05
Prolonged fever	24 (14.19)	4 (14.28)	> 0.05
Neurologic/psychiatric manifestations	16 (9.94)	2 (7.14)	< 0.05
Genital ulcers	8 (4.97)	2 (7.14)	< 0.05
Dysphagia	6 (3.73)	1 (3.57)	> 0.05
Sore throat	6 (3.73)	6 (21.43)	> 0.05
Abdominal pain	4 (6.78)	5 (38.48)	< 0.05
Amenorrhea	5 (3.11)		< 0.05
Chronic vaginal discharge	4 (6.78)		< 0.05
Chronic ear discharge	4 (2.48)		< 0.05
Splenomegaly	4 (2.48)		< 0.05
Hepatomegaly	8 (4.97)	2 (7.14)	< 0.05

Table 3. Characteristics of Diarrhea in 161 HIV Infected and 28 HIV Negative Patients with Chronic Diarrhea

Characteristic of diarrhea	Chronic diarrhea with HIV infection (n = 161)	Chronic diarrhea without HIV infection (n = 28)	p-Value
*3–6 bowel movements per day	101 (62.7)	24 (85.7)	< 0.05
* > 6 bowel movements per day	60 (37.3)	4 (14.3)	< 0.05
**Continuous diarrhea	25 (15.3)	2 (7.1)	< 0.05
Intermittent diarrhea	136 (84.5)	26 (92.9)	> 0.05
Liquid stool without blood or mucus	120 (74.5)	15 (53.6)	< 0.05
Semi liquid stools without blood or mucus	29 (18.0)	8 (28.6)	< 0.05
Stool with blood or mucus	12 (7.5)	5 (17.9)	> 0.05

Values are numbers of patients unless otherwise indicated. Percentages appear in parentheses. *At the time of assessment. **At least three or more liquid stools per day since onset of diarrhea.

tients (17.9%).

From these results it is apparent that diarrhea was more severe in the HIV infected patients than in the HIV negative group. This may be explained by the multifactorial etiology of HIV related diarrhea, including HIV itself¹¹⁾ (HIV enteropathy). Other opportunistic infections may be viral, bacterial, or fungal,¹²⁾ or malignancies,¹³⁾ bacterial overgrowth,¹⁴⁾ autonomic neuropathy,¹⁵⁾ and *clostridium difficile*¹⁶⁾ in antibiotic-treated patients.

Stool Microscopic Findings

Starch granules were observed in the stools of 149 HIV infected patients (92.6%) but in only 2 HIV negative ones (7.1%) as shown in Table 4. White blood cells were present in the stool of 18 HIV infected patients (11.2%) but in 7 HIV negative patients (25.0%).

The very high prevalence of starch granules in

the stools of HIV infected patients may be accounted for by a higher probability of HIV infected patients having malabsorption syndrome.¹⁷⁾ Maldigestion of carbohydrate is possible, because of hypochlorrydria which has been documented in AIDS patients.¹⁴⁾ Another possible explanation is the role of autonomic neuropathy.¹⁵⁾ This is well documented in HIV infected patients, with its attendant increase in gut motility and decrease in intestinal transit time, which in turn contributes to maldigestion and malabsorption.

The HIV negative patients had a proportionately higher frequency of fecal leukocytes than their HIV infected counterparts. This may be explained by the fact that HIV infected patients lack the ability to mount a strong mucosal inflammatory response because of their depressed immune system.

E. histolytica trophozoites with or without cysts were identified in 2 HIV infected patients (1.2%) but in none of the HIV negative patients (Table 4). *E.*

Table 4. Stool Microscopic Findings in Patients with Chronic Diarrhea

Stool finding	Chronic diarrhea with HIV infection (n = 161)	Chronic diarrhea without HIV infection (n = 28)	p-Value
Starch granules	149 (92.6)	2 (7.1)	< 0.05
White blood cells	18 (11.2)	7 (25.0)	> 0.05
Red blood cells	14 (8.7)	7 (25.0)	> 0.05
<i>E. histolytica</i> (trophozoite cyst)	2 (1.2)	—	< 0.05
<i>E. histolytica</i> (cyst only)	26 (16.1)	2 (7.1)	< 0.05
<i>Entamoeba coli</i>	5 (3.1)	1 (3.6)	> 0.05
<i>Giardia lamblia</i>	10 (6.2)	3 (10.7)	> 0.05
<i>Trichomonis hominis</i>	3 (1.9)	1 (3.6)	> 0.05
<i>Ascaris lumbricoides</i> (ova)	12 (7.5)	1 (3.6)	< 0.05
Hookworm (ova)	9 (5.6)	—	< 0.05
<i>Strongyloides stercoralis</i> (larvae)	7 (4.4)	—	< 0.05

Figures in parentheses = percentages.

histolytica cysts alone were present in 26 HIV negative patients (7.1%). Other protozoa identified were *Giardia lamblia*, *Entamoeba coli*, and *Trichomonas hominis*. No acid fast protozoon was identified. Non protozoal organisms identified were *Ascaris lumbricoides*, hookworm, and *Strongyloides stercoralis*.

The higher prevalence of *E. histolytica* cysts in the HIV infected group does not suggest that *E. histolytica* has a role in the etiopathogenesis of diarrhea in these patients. The presence of cysts alone in stool does not suggest pathogenicity. It is only when trophozoites are identified in fresh stool that a case for pathogenicity can be made. Studies have shown that AIDS patients may show high *Entamoeba coli* carriage without any corresponding increase in risk of invasive amoebiasis.^{18,19)} The explanation for this may be derived for the recent recharacterization of *E. histolytica* into non pathogenic and pathogenic species using isoenzyme analysis.^{20,21)} The nonpathogenic zymodemes have been shown to be common in the tropics and subtropics. Also, the classification of isolates from homosexual men in the U.K. and North America has to date shown them all belong to the nonpathogenic zymodeme.^{18,19)} Patients with AIDS may be deficient in mechanisms required to clear the cysts from the intestine.

It is interesting to note that of 489 stool samples examined in this study, no acid-fast protozoon was identified. Because of the known fact that cryptosporidiosis exhibits a striking seasonal variation in infection rate, with most of the infection occurring in the months of February to July,²²⁾ stool collection and examination in this study spanned a whole year to include all seasons (August 1996 to

October 1997) and yet not even one sample showed *Cryptosporidium* or any other acid-fast protozoon. Considering the immune state of the patients studied, any stool pathogen would have been present in large numbers and easily identifiable even without concentration methods. Published work on the role of acid-fast protozoa in the etiology of HIV related diarrhea is scarce in Nigeria. Chiria and his coworkers in Port Harcourt, Nigeria,²³⁾ found *Cryptosporidium* in 10.8% of 343 malnourished children less than 5 years of age with diarrhea using the modified ZN staining technique. A study in Ilorin Nigeria,²⁴⁾ designed to identify *Cryptosporidium* in the stool of patients with diarrhea showed a prevalence of 14%, but interesting these were all in-patients who were less than 8 years of age. *Cryptosporidium* was not identified in any patient 8 years of age or older. Both studies indicated that cryptosporidiosis may be a childhood problem in Nigeria. Since our study did not include pediatric patients with chronic diarrhea it is difficult to make conclusions on the epidemiology of cryptosporidiosis in Enugu at this stage. Children are, however, thought to be more susceptible to cryptosporidiosis because they are more likely to come in close physical contact with domestic animals as well as having lower personal hygiene standards than adults.

Studies in some parts of Africa and the developed countries showed that cryptosporidiosis is the most common cause of chronic diarrhea in HIV infected patients.²⁵⁻²⁸⁾ This may not be surprising because HIV related opportunistic infections are known to vary from locality to locality. A protozoa like *Pneumocystis carinii* is a very common opportunistic pathogen in HIV infected patients in the temper-

ate countries but has been found to be very rare in Africa.^{29,30)}

In conclusion, chronic diarrhea is common in HIV infection in Enugu. The microbial causes of this diarrhea may be markedly different from those reported in other parts of Africa and the developed world.

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