

## INTERNATIONAL REPORT

## Chronic Diarrhea Among Adults in Kigali, Rwanda: Association with Bacterial Enteropathogens, Rectocolonic Inflammation, and Human Immunodeficiency Virus Infection

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One hundred patients with chronic diarrhea were seen in the Department of Internal Medicine at the Centre Hospitalier de Kigali, Rwanda; stool and/or rectal swab culture was performed for these patients, and they underwent rectoscopy and serological testing for human immunodeficiency virus type 1 (HIV-1). Enteropathogenic bacteria were isolated from 39 (39%) of the patients: *Shigella* species (22 of 100 patients tested), non-*typhi* *Salmonella* (11/100), *Aeromonas* species (5/60), and *Campylobacter* species (4/60). Rectocolitis was seen in 70 (70%) of the patients. HIV-1 antibodies were detected in 82 (94%) of 87 patients tested. Cytomegalovirus was not found in rectal biopsy specimens from 29 patients. *Entamoeba histolytica* was detected in two of 31 rectal smears. Idiopathic ulcerative colitis was diagnosed for two HIV-1-seropositive patients. One or more AIDS-defining diseases were found in 32 (32%) of the patients, and 72 (72%) fulfilled the World Health Organization's clinical case definition criteria for AIDS. Chronic diarrhea, as seen in a hospital setting in a region highly endemic for HIV-1 infection, is strongly associated with HIV-1 infection, with rectocolonic inflammation, and with infection due to enteropathogenic bacteria.

Chronic diarrhea is one of the major complaints of patients with AIDS in developing countries. Reported prevalences among patients with AIDS vary from 25% to 90% [1]. In 1991 diarrhea was the chief complaint of 498 (11%) of 4,718 patients hospitalized in the Department of Internal Medicine at Centre Hospitalier de Kigali. The overall seropositivity rate for HIV type 1 (HIV-1) among all patients hospitalized in the Internal Medicine wards was 64%. However, it rose to 82% for all inpatients admitted with diarrhea [2]. This study evaluates the occurrence of HIV-1 infection, enteropathogenic bacterial infection, and rectocolonic mucosal inflammation in Rwandan adults with chronic diarrhea.

### Patients and Methods

From September 1991 until May 1992 and from October 1992 until March 1993, 100 consecutive patients >18 years of age with chronic diarrhea, mostly recruited from the inpatient Department of Internal Medicine at the Centre Hospitalier de

Kigali, were included in the study. Chronic diarrhea was defined as the production of at least 3 loose stools per day continuously for at least 1 month. Patients receiving antimicrobial treatment at the time of selection were excluded. After verbal consent was obtained, patients were screened for HIV-1 antibodies by means of an enzyme immunoassay (Vironostika; Organon Teknika, Boxtel, Netherlands).

Patients were classified at inclusion in the study according to the clinical case definition for AIDS established by the World Health Organization (WHO) [3], and past or present opportunistic diseases were recorded.

One or more fresh stool specimens or rectal swab specimens were collected from each patient. Specimens were cultured for *Salmonella*, *Shigella*, and *Yersinia* species (for 100 patients) and for *Campylobacter* and *Aeromonas* species (for 60 patients), by means of recommended methods [4]. Identification and susceptibility testing of pathogens were performed according to standard procedures.

Rectosigmoidoscopy with use of a rigid rectoscope was performed on all patients after they defecated. Abnormal rectal mucosa was graded as congestive, ulcerative and/or hemorrhagic, or aphthous. For patients with ulcerative, hemorrhagic, or aphthous lesions, a rectal biopsy specimen was examined for cytomegalovirus intracellular inclusion bodies, and a fresh mucosal smear sample was examined for hematophagous trophozoites of *Entamoeba histolytica*. A diagnosis of idiopathic ulcerative colitis was retained only for patients with crypt abscesses in the rectal biopsy specimen whose stool cultures were

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**Table 1.** Results of stool and/or rectal swab culture, mucosal smear microscopy, and histology for 100 patients from Kigali, Rwanda, who had chronic diarrhea.

Finding	Percent of patients tested
Bacterial enteropathogens	39
<i>Salmonella</i> species (n = 100)	11
<i>Shigella</i> species (n = 100)	22*
<i>Campylobacter</i> species (n = 60)	4
<i>Aeromonas</i> species (n = 60)	5†
Amoebic colitis (n = 31)	2
Cytomegalovirus colitis (n = 29)	0
Chronic idiopathic inflammatory bowel disease (n = 100)	3‡

\* Including one mixed infection with *Salmonella* species.  
 † Including one mixed infection with *Salmonella* species and one with *Campylobacter* species.  
 ‡ Including two cases of idiopathic ulcerative colitis and one of Crohn's colitis.

negative and who did not respond to treatment with antibiotics and metronidazole but whose condition improved markedly with corticosteroid therapy.

**Results**

One hundred patients (66 males [mean age, 34.4 years] and 34 females [mean age, 30.3 years]) with chronic diarrhea were studied. The WHO's criteria for the clinical case definition of AIDS were met by 72 patients. At least one AIDS-defining disease was present in 32 patients, including esophageal candidiasis (22 patients), extrapulmonary tuberculosis (6), generalized Kaposi's sarcoma (4), cryptococcal meningitis (2), and non-typhi *Salmonella* bacteremia (2). Serological results for HIV-1 were available for 87 patients, of whom 82 (94%) were HIV-1-seropositive.

Microbiological and parasitological results are shown in table 1. Of 246 stool samples collected (mean, 2.4 samples per patient), only 50 (20%) were culture-positive for bacterial enteropathogens, whereas 8 (54%) of 15 rectal swab cultures were positive, all for *Shigella* species. At least one bacterial enteropathogen was found in 39 patients (39%). Non-typhi *Salmonella* was isolated from 11 patients (11%) and *Shigella* species from 22 (22%); the *Shigella* species included *S. flexneri* (15), *S. sonnei* (3), *S. boydii* (1), and *S. dysenteriae* serotypes 3–10 (1). Two isolates were not subtyped. Mixed infection with *Salmonella* and *Shigella* species was found in one patient (1%). *Campylobacter* species were seen in 4 (7%) of 60 patients and *Aeromonas* species in 5 (8%) of 60; 2 of the latter 4 patients had mixed infections (1 with *Campylobacter* species and 1 with *Salmonella* species).

Obvious signs of rectocolonic inflammation were seen in 70 patients (70%), of whom 39 had congestive rectocolitis (often with purulent mucus), 29 had hemorrhagic and/or multiple ul-

cerative mucosal lesions, and 2 had aphthous lesions. Rectocolonic inflammation was seen in 34 (87%) of 39 patients demonstrated to be infected with bacterial enteropathogens—including 8 of 11 (72%) infected with *Salmonella* species and 20 of 22 (91%) infected with *Shigella* species—but in only 36 (59%) of 61 patients who were culture-negative ( $\chi^2$ ,  $P < .001$ ).

Cytomegalovirus inclusion bodies were not seen in any of the 29 mucosal biopsy samples taken. Hematophagous trophozoites of *E. histolytica* were seen in only two of 31 cases. In four patients, all HIV-1-seropositive, crypt abscesses were present in colonic mucosa, suggesting idiopathic ulcerative colitis. Two of these also had inflammatory rectal pseudopolyps. A definite diagnosis ultimately was retained for only two patients. For another patient, who was HIV-1-seronegative, histology was compatible with Crohn's disease.

Among 5 HIV-1-seronegative patients included in this study, bacterial enteropathogens were isolated from 2, and obvious rectoscopic inflammation was seen in 4.

**Discussion**

As many studies have clearly shown, chronic diarrhea is strongly associated with HIV-1 infection in sub-Saharan Africa [1, 5–8]. This is also seen in Kigali, where the HIV-1 seroprevalence among the adult urban population reaches 30% [9]. Most patients in this study showed clinical signs associated with an advanced immunodeficiency status. Although not specific, the mucosal lesions were compatible with bacterial enterocolitis and also were significantly more frequently seen in patients demonstrated to be infected with enteropathogenic bacteria, especially *Shigella* species. Neither cytomegalovirus infection nor amoebic colitis could be responsible for these lesions, but chronic idiopathic inflammatory bowel disease must be considered as a potential cause.

The patient population studied by Colebunders et al. in Kinshasa, Zaire, was similar to ours in many respects, but the reported prevalence of bacterial enteropathogens was strikingly lower than in this study [1, 5]. Since salmonellosis and endemic shigellosis are widespread throughout sub-Saharan Africa, and since HIV-seropositive patients tend to have recurrent or persistent bacterial enteritis [10, 11], one might expect a greater impact of these pathogens on the pathology associated with HIV-1-positive African patients. Moreover, symptomatic (HIV-seronegative) adult carriers of *Shigella* species are rare [12]. Repeating the procedures and performing a rectal swab culture substantially improve the overall culture yield. *Campylobacter* and *Aeromonas* species are also worth looking for [11]. It is therefore more likely that culture performance in previous studies has been poor.

Rectosigmoidoscopy with use of a rigid rectoscope is a sensitive, reliable, and safe diagnostic procedure that can usefully orient the diagnostic workup for chronic diarrhea.

Although there is ample evidence that the etiology of chronic diarrhea in HIV-infected African individuals is multifactorial,

bacterial enteritis should not be ignored, as it is widespread and potentially treatable. First-line therapy has to be redirected toward effectively treating bacterial enterocolitis by means of appropriate antibiotic regimens.

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