COLONOSCOPIC FINDINGS IN HIV-INFECTED PATIENTS WITH CHRONIC DIARRHOEA AND NEGATIVE STOOL ANALYSIS AT KENYATTA NATIONAL HOSPITAL

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BACKGROUND

• ~ 42M HIV infected persons worldwide.
• 29M (69%) from sub-Saharan Africa
• In Kenya, ~1.5M people living with HIV\(^1\).
• HIV mortality, 150,000 per annum in Kenya\(^1\).
• Chronic diarrhoea occurs in 60-70% of HIV-infected individuals in developed countries and in 80-90% in the developing countries\(^2\).

Literature review (1)

• HIV-related morbidity accounts for 70% of the admissions at KNH (highest), and of these, 10% present with chronic diarrhoea.

• Currently, 40 to 50 patients on average are admitted daily into the medical wards at KNH, and of these, about 3 to 5 patients present with chronic diarrhoea in HIV infection.
The mechanisms involved in HIV-related chronic diarrhoea are multifactorial, involving the interplay of opportunistic infections, malabsorption of nutrients, reduced food intake, metabolic alterations, and tissue damage inflicted by HIV itself\textsuperscript{3,4}.

Literature review (3)

• Infectious aetiologies account for 30-80% of HIV-associated diarrhoea; finding an aetiological pathogen depends on the extent of diagnostic evaluation, from stool studies to colonoscopy with subsequent histological evaluation of biopsy tissue\textsuperscript{5}.

• Commonest pathogens- CMV, C. parvum, M.TB, Mycobacterium avium-complex.

• Moturi et al: 36.8% prevalence of intestinal parasitic infections in HIV seropositive patients with chronic diarrhoea at KNH\textsuperscript{6}. C. parvum identified in 11%.


\textsuperscript{6} Moturi et al. Intestinal parasitic infections in HIV patients with chronic diarrhoea at KNH (2006).
Literature review (4)

• However, despite extensive stool studies, no aetiological pathogen is identified in 15-50% of HIV-infected patients with chronic diarrhoea.

Literature review (5)

- Mwachari et al. 1992: identified a pathogen in 52% of HIV seropositive patients at KNH after extensive stool studies (microscopy, bacterial & mycobacterial cultures). He recommended colonic biopsies with histology to increase the yield.

- Cello et al. 1996 (USA): Colonoscopy performed in 79 patients with chronic HIV-related diarrhoea and negative stool studies identified an aetiological pathogen in 27.8%.

Literature review (6)

• However, in their prospective study of 155 patients with HIV-related diarrhoea, Blanshard et al. found that 67.3% had diffuse chronic inflammation in the absence of a specific pathogen\textsuperscript{10}.

• In a similar study by Hing MC, colonic biopsies revealed diffuse colitis characterized principally by a mixed inflammatory cell infiltrate (mononuclear cells, lymphocytes and neutrophils). No other aetiiological pathogens were found\textsuperscript{11}.


STUDY JUSTIFICATION

• Despite extensive stool studies, no aetiological pathogen is identified in 15-50% of patients with HIV-related chronic diarrhoea (Cello, 1997).

• Our study sought to identify whether any additional findings derived from colonoscopy and histological evaluation of biopsy tissue in HIV-infected patients with negative stool results will add to our knowledge of the aetiological features and pathogens of HIV-associated diarrhoea.
Study justification (2)

• No such data is available locally and the findings from this study enabled us to compare our data with that from other regional and international studies.
Study Question

- What additional data regarding aetiological pathogens and features of colonic mucosa in HIV-infected patients with chronic diarrhoea and negative stool results shall we obtain by performing colonoscopy and histological evaluation of biopsy tissue?
BROAD OBJECTIVE

• To describe the macroscopic and microscopic findings in HIV seropositive patients with stool negative chronic diarrhoea at colonoscopy and following histological evaluation of biopsy tissue.
SPECIFIC OBJECTIVES

1. To describe the macroscopic findings at colonoscopy in HIV-infected patients with chronic diarrhoea and negative stool analysis at KNH.

2. To identify by histology, the aetiological features and pathogens of chronic diarrhoea in HIV seropositive patients with negative stool analysis at KNH.

3. To describe the WHO clinical stage of HIV disease of the patients, the CD4+ T-cell counts and the colonoscopic and histopathological features.
METHODOLOGY

• Study Design
  - A descriptive cross-sectional study
• Study site
  - Kenyatta National Hospital (KNH); medical wards
• Study population
  Patients admitted with chronic diarrhoea, who tested positive for HIV infection and had negative stool analysis
Case definition

• **Chronic diarrhoea:** 3 or more loose stools passed daily (in a 24 hour period) for a duration of 4 or more weeks.

• **Negative stool analysis:** One stool specimen from which no enteric pathogen or parasite has been identified following:
  (i) microscopic examination for ova and cysts
  (ii) culture on SS (Salmonella/Shigella) medium
Methodology (2)

Patient selection

Inclusion criteria:

Patients who were HIV seropositive and
(i) presented with chronic diarrhoea
(ii) had negative stool analysis
(iii) were aged 18 years and above

Patients who were willing to participate in the study, abide by the protocol requirements and undergo colonoscopy were included in the study after signing an informed and written consent.
Methodology (3)

Sampling technique

- Consecutive sampling of patients admitted with chronic diarrhoea, who tested positive for HIV infection and had negative stool results was done until the desired sample size of 54 patients was achieved.
Methodology (4)

Recruitment

- The PI visited post-admission medical wards, screened patients admitted with chronic diarrhoea and picked those with confirmed HIV seropositive status.
- Patients with unknown HIV status were tested upon consent. Those with seropositive status were selected after post-test counselling.
- Stool analysis, facilitated by the PI, was done as part of the routine ward work-up in HIV-infected patients with chronic diarrhoea.
- Patients with negative stool results were recruited to undergo colonoscopy once consent was given.
Methodology (5)

Data collection

- **Clinical methods**
  - Demographic data and history was taken and entered into a study proforma.
  - A complete physical examination was performed, and patients classified as per the WHO clinical staging system for HIV infection and disease.
  - Bowel preparation was done as per standard procedure and thereafter, colonoscopy was performed under light sedation.
  - At colonoscopy, all the macroscopic features were noted and graded according to a standard scoring scale.
Standard scoring scale for mucosal abnormalities

• **Grade 0**: normal mucosa
• **Grade 1**: abnormal erythema, oedema and/or loss of normal vascular markings
• **Grade 2**: erosions or friability
• **Grade 3**: gross ulcerations >5mm diameter, inflammatory pseudopolyps, nodules or spontaneous haemorrhage

Methodology (6)

• Colonoscopy

- 2 mucosal biopsies were taken from each of the following sites: ileo-caecal junction, proximal ascending colon, recto-sigmoid area, the rectum and anal region.
- additional biopsies were taken from sites with detectable and/or suspicious lesions.
- Biopsy specimens were placed and fixed in 10% buffered formalin in separate labelled bottles and transported to the Nairobi Hospital laboratory.
Methodology (7)

• Laboratory methods
  - Venous blood 5mls was drawn from all the patients for HIV screening and CD4 count

• Histopathology:
  - The fixed biopsy specimens were impregnated and embedded in paraffin wax, then sectioned
  - Specimens were subjected to H & E, Z-N, Periodic Acid-Schiff and Grocott-methenamine silver stains.
  - An experienced histopathologist together with the PI read the histology slides.
DATA ANALYSIS

• Data was collected using the study proforma and analyzed using SPSS version 12 package.
• Descriptive analysis was done using frequency distribution for categorical variables such as gender and histology results.
• Descriptive analysis for Continuous variables such as age, CD4 count, duration and frequency of diarrhoea was done using measures of central tendency and dispersion.
• Independent T-test was to determine difference in mean for continuous variables.
• Chi-square test and Fischer Exact test was used to determine associations of categorical variables.
• Significance levels at $p=0.05$
RESULTS

• The study was conducted between September 2006 and October 2007.
• Patients were recruited from the medical wards at KNH.
• 159 patients with chronic diarrhoea were screened; 70 patients met the inclusion criteria, of whom 16 were excluded (12 were too sick to undergo colonoscopy and in 4, the scope was defective).
• 54 patients underwent colonoscopy and histological evaluation of biopsy tissue.
CHRONIC DIARRHOEA > 4 WKS DURATION (159)

HIV Negative
(31 pts. Excluded)

HIV Positive
(128 patients)

Negative Stool studies
(70 patients)

16 patients excluded
12 too sick
4 defective scope

54 patients scoped

(58 patients excluded)

37 Positive stool results
8 refused to give consent.
13 refused to abide by protocol requirements.
Age and gender distribution

- Of the 54 patients, 28 (51.9%) were male and 26 (48.1%) were female, M:F ratio of 1:1.
- Mean age was 35.43 yrs ±11.94 (95% CI, 32.17 to 38.69) with a range of 19 to 71 yrs.
- Mean age of the male patients was 36.46 yrs and that of the female patients 34.31 yrs (p=0.407).
- Median age was 33.50 yrs.
## Demographic Characteristics

<table>
<thead>
<tr>
<th>Variables</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>28</td>
<td>51.9%</td>
</tr>
<tr>
<td>Female</td>
<td>26</td>
<td>48.1%</td>
</tr>
<tr>
<td>Mean age (35.43yrs)</td>
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<td></td>
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<tr>
<td><strong>Residence</strong></td>
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<td></td>
</tr>
<tr>
<td>Urban</td>
<td>37</td>
<td>68.5%</td>
</tr>
<tr>
<td>Rural</td>
<td>17</td>
<td>31.5%</td>
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<tr>
<td><strong>Marital status</strong></td>
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<tr>
<td>Married</td>
<td>29</td>
<td>53.7%</td>
</tr>
<tr>
<td>Single</td>
<td>6</td>
<td>11.1%</td>
</tr>
<tr>
<td>Divorced/separated</td>
<td>12</td>
<td>22.2%</td>
</tr>
<tr>
<td>Widowed</td>
<td>7</td>
<td>13.0%</td>
</tr>
<tr>
<td><strong>Educational level</strong></td>
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<td></td>
</tr>
<tr>
<td>None</td>
<td>2</td>
<td>3.7%</td>
</tr>
<tr>
<td>Primary</td>
<td>33</td>
<td>61.1%</td>
</tr>
<tr>
<td>Secondary</td>
<td>16</td>
<td>29.6%</td>
</tr>
<tr>
<td>College/ Polytechnic</td>
<td>2</td>
<td>3.7%</td>
</tr>
<tr>
<td>University</td>
<td>1</td>
<td>1.9%</td>
</tr>
<tr>
<td><strong>Occupation status</strong></td>
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<td></td>
</tr>
<tr>
<td>Unemployed</td>
<td>21</td>
<td>38.9%</td>
</tr>
<tr>
<td>Business persons</td>
<td>18</td>
<td>33.3%</td>
</tr>
<tr>
<td>Casual</td>
<td>5</td>
<td>9.3%</td>
</tr>
<tr>
<td>Professionals</td>
<td>2</td>
<td>3.7%</td>
</tr>
<tr>
<td>Others</td>
<td>8</td>
<td>14.8%</td>
</tr>
</tbody>
</table>
Characteristics of diarrhoea

Duration of the diarrhoea
• The mean duration of the diarrhoea was 9.31 weeks, with a range of 4 to 78 weeks.
• The median duration was 6 weeks.

Frequency of diarrhoeal episodes
• The mean frequency of the diarrhoeal episodes was 5.56 episodes, with a range of 3 to 10 episodes in a 24 hour period.
• The median frequency was 5.5 episodes.
• Majority of the patients (83.4%) had 4 to 6 episodes in a 24 hour period.
Clinical characteristics of the study population

• All the 54 patients (100%) presented with weight loss and fatigue.
• Marked weight loss >10% of the previous body weight and intermittent fever of >1 month’s duration were present in 94.4% and 96.3%.
• Other clinical features at presentation were oral thrush in 75.9%, Kaposi’s sarcoma in 9.26%, cryptococcal meningitis in 5.56% and pulmonary TB in 20.37%.
Clinical characteristics of the study population

<table>
<thead>
<tr>
<th>Condition</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seborrhoea</td>
<td>13.0%</td>
</tr>
<tr>
<td>Onychomycosis</td>
<td>14.8%</td>
</tr>
<tr>
<td>Herpes zoster</td>
<td>16.7%</td>
</tr>
<tr>
<td>Angular cheilitis</td>
<td>25.9%</td>
</tr>
<tr>
<td>Pallor</td>
<td>42.6%</td>
</tr>
<tr>
<td>Oral thrush</td>
<td>75.9%</td>
</tr>
<tr>
<td>Post Infl dermatosis</td>
<td>79.6%</td>
</tr>
<tr>
<td>Lymphadenopathy</td>
<td>83.3%</td>
</tr>
<tr>
<td>Hypotension</td>
<td>92.6%</td>
</tr>
<tr>
<td>Dehydration</td>
<td>94.4%</td>
</tr>
<tr>
<td>Wasting</td>
<td>94.4%</td>
</tr>
<tr>
<td>Fever</td>
<td>96.3%</td>
</tr>
</tbody>
</table>
Clinical staging of HIV infection and CD4+ T-cell counts

- Forty one patients (75.9%) were in WHO clinical stage 4 while thirteen (24.1%) were in stage 3.
- The mean CD4+ cell count was 135.52 cells/mm³, with a range of 2 to 653 cells/mm³.
- The mean CD4+ cell count of the male patients was 161 cells/mm³ and that of the female patients was 108.08 cells/mm³ (p= 0.139)
- Twice as many female patients (69.2%) as males (35.7%) had CD4+ cell counts <100 cells/mm³.
<table>
<thead>
<tr>
<th>CD4 Count (cells/mm³)</th>
<th>MALE N=28 (%)</th>
<th>FEMALE N=26(%)</th>
<th>TOTAL N=54(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;50</td>
<td>8 (28.6%)</td>
<td>9 (34.6%)</td>
<td>17 (31.5%)</td>
</tr>
<tr>
<td>51-100</td>
<td>2 (7.1%)</td>
<td>9 (34.6%)</td>
<td>11 (20.4%)</td>
</tr>
<tr>
<td>101-200</td>
<td>10 (35.7%)</td>
<td>4 (15.4%)</td>
<td>14 (25.9%)</td>
</tr>
<tr>
<td>201-350</td>
<td>6 (21.4%)</td>
<td>3 (11.5%)</td>
<td>9 (16.7%)</td>
</tr>
<tr>
<td>&gt;350</td>
<td>2 (7.1%)</td>
<td>1 (3.8%)</td>
<td>3 (5.6%)</td>
</tr>
</tbody>
</table>
## WHO clinical stage and CD4 count

<table>
<thead>
<tr>
<th>WHO Clinical stage of HIV</th>
<th>CD4 COUNT</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;50</td>
</tr>
<tr>
<td>Stage 3</td>
<td>0</td>
</tr>
<tr>
<td>Stage 4</td>
<td>17</td>
</tr>
</tbody>
</table>
## Comparison of Body Mass Index between WHO clinical stage 3 and 4

<table>
<thead>
<tr>
<th>Clinical HIV Stage</th>
<th>Mean</th>
<th>N</th>
<th>Std. Deviation</th>
<th>Median</th>
<th>Minimum</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 3</td>
<td>19.27</td>
<td>13</td>
<td>3.13</td>
<td>18.72</td>
<td>14.50</td>
<td>27.18</td>
</tr>
<tr>
<td>Stage 4</td>
<td>15.02</td>
<td>41</td>
<td>3.44</td>
<td>14.87</td>
<td>9.67</td>
<td>25.07</td>
</tr>
<tr>
<td>Total</td>
<td>16.04</td>
<td>54</td>
<td>3.81</td>
<td>16.13</td>
<td>9.67</td>
<td>27.18</td>
</tr>
</tbody>
</table>

Mann Whitney U-test: $Z = -3.682$: $P < 0.01$ (0.000) significant difference in BM1.
Anti-retroviral therapy

• Only 12 patients (22.2%) were on anti-retroviral therapy.

• The most common regime was Stavudine, Lamivudine and Efavirenz in 6 patients.

• Four patients had defaulted treatment, 2 restarted the drugs within two months and 2 were lost to follow-up till re-admission.
Prior Antibiotic use

- Use of antibiotics four weeks prior to the colonoscopy was documented in 47 patients (87%), 23 males and 24 females.
- The most commonly used antibiotic was metronidazole in 80.85% (38 pts) and Trimethoprim/sulphamethoxazole in 68.09% (32 pts).
- Use of Trimethoprim/sulphamethoxazole as prophylaxis was noted in only 18 patients (33.3%).
- Majority of the patients were on >1 antibiotic simultaneously.
Distribution of antibiotic use in the study population

- Norfloxacin: 55.32%
- Ciprofloxacin: 19.15%
- TRI/SMX: 68.09%
- Metronidazole: 80.85%
- Augmentin: 6.38%
- Erythromycin: 4.26%
MACROSCOPIC FINDINGS
Colonoscopic findings in the study population based on the standard scoring scale for mucosal abnormalities

<table>
<thead>
<tr>
<th>Standard scoring scale</th>
<th>Description</th>
<th>frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 0</td>
<td>Normal mucosa</td>
<td>8</td>
<td>14.8%</td>
</tr>
<tr>
<td>Grade 1</td>
<td>Abnormal erythema, oedema and/or loss of normal vascular markings</td>
<td>15</td>
<td>27.8%</td>
</tr>
<tr>
<td>Grade 2</td>
<td>Erosions or friability</td>
<td>18</td>
<td>33.3%</td>
</tr>
<tr>
<td>Grade 3</td>
<td>Gross ulcerations &gt;5mm diameter inflammatory polyps, nodules or spontaneous hemorrhage</td>
<td>13</td>
<td>24.1%</td>
</tr>
</tbody>
</table>
Outstanding colonoscopic features

• Seven patients had features in keeping with ulcerative colitis with gross ulcerations > 5mm in diameter covering the entire colon, marked mucosal wall oedema and haemorrhage.

• One patient had an ulcerated haemorrhagic tumour (5×3cm) at rectosigmoid junction

• Florid anorectal candidiasis with ulceration over caecum in 1 patient

• Nodular colitis with erosions in the caecum and large shallow ulcer with irregular margins in the transverse colon in 2 patients

• Microabscesses in the distal rectum in 6 patients
HISTOLOGICAL FINDINGS

- All the study patients (100%) had diffuse non-specific chronic colitis, which varied in severity from mild to severe.
- Atrophic mucosal changes were present in 61.1%.
- Only 1 patient had evidence of infectious pathology on histology, with ovoid schistosomal ova with lateral spines surrounded by multi-nucleated giant cells noted.
- Other histological findings were mucosal haemorrhage in 48.1%, ulcerative colitis in 22.2% and apoptosis of mucosal elements in 25.9%.
Histological findings in the Study population

- Chronic active colitis: 90.70%
- Crypt abscesses: 61.10%
- Atrophy: 48.10%
- Mucosal haemorrhage: 34.20%
- Atypia: 25.90%
- Ulcerative colitis: 25.90%
- Fibrioid necrosis: 22.20%
- Fatty changes: 16.70%
- Malakoplakia: 7.40%
- Polyposis: 3.70%
- Infections: 1.90%
- Tumor: 1.90%
- Atrophy: 1.90%
Diffuse colitis in all patients (100%)
Mucosal atrophy in 33 patients (61.1%)
Crypt abscesses with severe colitis in 49 patients (90.7%)
Severe ulcerative colitis in 12 patients (22.2%)
Crypt destruction and distortion in severe colitis
Ova of Schistosoma mansoni in 1 patient
Ova of S. Mansonii surrounded by inflammatory cells
Fatty changes (steatosis) in 5 patients (9.3%)
Submucosal steatosis in 5 patients (9.3%)
Apoptotic bodies within the crypts in 14 patients (25.9%)
Apoptotic changes

Normal crypt
Cannibalism noted in 5 patients (9.3%)
DISCUSSION

• All the study patients (100%) had diffuse non-specific chronic colitis, varying in severity from mild to severe. The cellular infiltrate was comprised predominantly of chronic inflammatory cells (plasma cells and lymphocytes).

• Forty nine patients (90.7%) had suppurative crypt abscesses with numerous crypt inclusions and neutrophilic infiltrates.

• The patients with CD4+ counts< 50 cells/mm³ had florid suppurative colitis with mucosal ulceration, extensive destruction and disorganisation of crypt architecture. They were also noted to have more extensive mucosal atrophy as compared to patients with higher CD4+ counts > 200 cells/mm³.
Discussion (2)

- Blanshard studied 155 patients with HIV-related diarrhoea and 67.3% had diffuse chronic colitis in the absence of a specific pathogen\(^\text{10}\).
- In a similar study by Hing MC, colonic biopsies revealed diffuse colitis characterised principally by a mixed inflammatory cell infiltrate (lymphocytes, plasma cells and neutrophils)\(^\text{11}\).
- HIV nucleic acid was identified by in situ hybridization in 70% of the biopsies, and in 60% of them, presence of HIV DNA was confirmed by Southern blot analysis. It was concluded that the mucosal changes were as a direct result of HIV infection on the gut. No other infectious pathogen was identified\(^\text{11}\).

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Discussion (3)

- Mucosal atrophy was found in 61.1% of our study patients. The crypts were abnormally elongated in 90% of the tissue sections. This finding is documented in several studies and has been implicated in the aetiology of HIV-related diarrhoea.

- Zambia study- Morphometric studies of colonic and jejunal mucosal tissue showed that T-cell activation induces an enteropathy in HIV infection characterised by villous atrophy, crypt hyperplasia and mucosal destruction leading to increased crypt depth and reduced villous height\(^\text{12}\).

• Kotler demonstrated widespread colonic mucosal atrophy and apoptosis in 168 patients. Biopsy tissue subjected to PCR, and immuno- histochemical staining detected viral DNA in 70%. Immunohistologic studies using monoclonal antibodies to HIV p24 antigen were positive in 80%, with elevated tissue contents of HIV p24, IL-1 and TNF\textsuperscript{13}.

• Mucosal atrophy and apoptosis postulated to be the cause of the chronic diarrhoea was attributed to HIV infection.

Discussion (5)

• Apoptosis of the mucosal elements was noted in 25.9% of our study patients within the lamina propria and apoptotic bodies were seen within the crypts, with increased lymphocytes and plasma cells.

• Uganda study- histomorphometric studies on biopsy tissue showed severe flattening of villi, atrophy and apoptotic bodies in the crypt epithelium in 90%. HIV-infected cells were seen in 80% of the biopsies after incubation with primary monoclonal antibodies\textsuperscript{14}.

Discussion (6)

• Only one patient had evidence of infection, with ovoid schistosomal ova with lateral spines in the colonic mucosa surrounded by multi-nucleated giant cells and granulomatous reaction.

• The absence of opportunistic infections may be attributed to the indiscriminate use of antibiotics in our study population, of whom 87% were on antibiotics.
Discussion (7)

• Related studies have shown that HIV-infected patients are at high risk of infection with toxin-producing strains of *Clostridium difficile* due to frequent hospitalisation and exposure to antibiotics, resulting in chronic unresolving diarrhoea.

• An exponential increase in the frequency of *Clostridium difficile*-associated diarrhoea was reported by Starr et al. who reported the infection in 13% of HIV seropositive patients with chronic diarrhoea in the United States\(^\text{15}\).

• Willingham in a similar study in Peru also noted increased prevalence of *C. difficile* –associated diarrhoea in HIV patients and this was associated with 6-fold increase in mortality\(^\text{16}\).


Discussion (8)

• Another peculiar feature noted in 9.3% of patients was ‘cannibalism’, whereby some mucosal glands are adsorbed into others, a feature found in disease processes that evoke severe chronic inflammation.

• One patient had an ulcerated haemorrhagic mass at the recto-sigmoid junction, shown by histology to be a moderately differentiated adenocarcinoma.
Submucosal steatosis of the colon was present in 9.3% of our patients.

Another postulated cause of HIV-related diarrhoea is gp 120-induced Bob activation (a co-receptor for HIV expressed on intestinal mucosa).

Kotler et al. performed RNA insitu hybridization and immunostaining of colonic mucosa, calcium flux studies and microtubule staining\(^{17}\).

Gp 120 induced Bob activation was demonstrated to cause calcium signalling and microtubule loss, resulting in reduced enterocyte lipid transport and thus, lipid malabsorption, steatosis of submucosal tissue, increased paracellular permeability and resultant chronic diarrhoea.

CONCLUSIONS

• The findings from this study demonstrated clearly that colonoscopy is a valuable diagnostic tool in the evaluation of stool-negative chronic diarrhoea in HIV infection. Histological evaluation of the biopsy tissue taken at colonoscopy revealed that various colonic mucosal changes are present in these patients in the absence of OI, and these are thought to be as a result of tissue damage inflicted by HIV itself.

• Chronic inflammation of the intestinal mucosa with no identifiable pathogens in HIV infected patients with chronic diarrhoea is a common finding. These patients are likely to have non-specific inflammatory changes with mucosal atrophy upon evaluation. This was evident in our study patients who were noted to have non-specific chronic colitis with mucosal atrophy, ulceration, haemorrhage and apoptotic features upon histological evaluation.
• Colonoscopy is essential for adequate diagnosis and institution of appropriate treatment among patients with chronic diarrhoea in HIV infection as multiple pathologies, both infectious and non-infectious, may coexist together and have similar presentations.
Study Limitations

• Due to financial constraints, extensive investigations were not performed on the biopsy tissue to exhaustively identify the causes of chronic diarrhoea namely, mycobacterial and fungal cultures, PCR technique and immunohistochemical staining to isolate viral aetiologies.

• Use of antimicrobials prior to colonoscopy may have reduced the yield of infectious agents.

• The patients studied were in stages 3 and 4 of HIV/AIDS disease. Eligible patients were excluded due to their moribund condition and these may have had an impact on the results.

• Only one stool sample was analysed from each patient and this may have reduced the yield of the infectious pathogens isolated.