

Prevalence of gastrointestinal symptoms among ambulatory HIV patients and a control population

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Abstract

Background The gastrointestinal tract is a common site of involvement in HIV-infected patients. Gastrointestinal symptoms are common in the general population and are associated with decreased quality of life.

Methods Ambulatory consecutive HIV-infected patients and consecutive healthy blood donors seen in Jamaica were studied. A 19-item questionnaire of GI symptoms was administered.

Results There were 196 respondents. Among 99 HIV patients, the mean number of symptoms was 2.9 and in 97 controls 3.3 ($p=0.091$). Dysphagia and odynophagia were present in 8.1% of HIV patients and 3.1% of the controls ($p=0.129$). Belching was present in 59.6% of HIV patients and in 96.8% of controls ($p\leq 0.001$). In the control group, 44.3% had heartburn compared to 29.3% of HIV patients. Within the preceding year, 26.3% of HIV participants and 12.4% of controls sought medical attention for their GI symptoms ($p=0.001$). GI symptomatology was directly related to immune status in the HIV group as patients with a CD4 count of less than 200 cells/ μL reported up to 6 GI symptoms, those with CD4 of 201-350 cells/ μL had 3 symptoms, and patients with CD4 greater than 351 cells/ μL had 1 symptom. Pain on swallowing, and vomiting were significantly more common in patients with CD4 <350 cells/ μL than in controls.

Conclusions GI symptoms were common in HIV patients and controls. In HIV patients symptoms were directly related to CD4 count. Pain on swallowing and vomiting were significantly more common in patients with CD4 <350 cells/ μL than in controls.

Keywords GI symptoms, HIV infection

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Introduction

Human immunodeficiency virus (HIV) infection has grown to pandemic proportions with an estimated 65 million infections and 25 million deaths worldwide. Sub-Saharan Africa carries the overwhelming burden, having 67% of the world's HIV population [1]. This is followed by the Caribbean where there are an estimated 230,000 HIV-infected persons, with national prevalence rates surpassing 1% [2]. The epidemic

however appears to have stabilized in Jamaica, with a national adult HIV prevalence of 1.6% over the last few years [3]. Continuous research into various aspects of HIV/AIDS, including its varying clinical manifestations is needed for better understanding of this disease.

It is known that the gastrointestinal (GI) tract is a common site of involvement in HIV-infected patients at various stages of their disease. These GI manifestations may be debilitating and include anorexia, dysphagia, vomiting, weight loss and diarrhea [4]. Previous studies have shown that opportunistic infections, neoplasms, inflammatory changes and direct mucosal invasion of the GI tract by HIV, are well recognized causative factors [5]. Additionally, patients with significant immunosuppression as evidenced by CD4 counts less than 500 cells/ μL , are more likely to develop these GI symptoms. However, antiretroviral treatment can improve immune function, leading to fewer GI symptoms [6,7].

Investigation of the various GI manifestations in HIV patients has not been explored in the Jamaican population. This study investigated the prevalence of common GI symptoms in

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the ambulatory HIV-infected population compared to those seen in a healthy population of blood donors not known to have HIV infection.

Materials and Methods

A single-center, quantitative, cross-sectional, study was performed. Ambulatory consecutive HIV-infected patients seen at the Center for HIV/AIDS Research, Education and Services (CHARES) and consecutive healthy blood donors at the blood bank of the University Hospital of the West Indies (UHWI), Jamaica were studied. CHARES is a non-profit outpatient facility at the UHWI which provides medication, counseling, nutritional support and medical care to HIV-infected patients. Currently it serves over 800 patients. The study was approved by the (UHWI/UWI) Faculty of Medical Sciences Ethics committee.

Inclusion criteria for eligibility for the study were:

a) patients over the age of 18 years; b) confirmed HIV-positive status regardless of duration; c) male or non-pregnant female patients of the CHARES clinic; and d) attending CHARES during days of clinic operation only. The control group consisted of: a) participants over the age of 18 years; b) male or non-pregnant females; and c) donors to the UHWI Blood Bank during the days of the UHWI Blood Donor operation only. Exclusion criteria were: a) patients assessed as needing emergency care and in-patients of the hospital (UHWI); b) patients of the gastroenterology clinic and all other outpatient clinics; c) pregnant females; and d) children under the age of 18 years.

Participants in the study were interviewed by one of the study investigators who explained the purpose of the study, obtained informed consent and administered the questionnaire. The questionnaire was administered individually in order to ensure patients' confidentiality (Appendix).

Patients in the HIV group were ambulatory consecutive patients of the CHARES clinic. They were invited to participate in the study by one of the investigators, not involved in the management of the patient on the day of recruitment. Patients were eligible for the study regardless of the stage of their disease.

Consecutive blood donors of the UHWI Blood Bank were interviewed in the unit's waiting room on the days of blood bank operation. They were invited to participate in the study by one of the investigators. The participants from the control group were matched for age and gender with the HIV group.

Participants in each study group were asked to answer a questionnaire of GI symptoms administered by the investigator. The study instrument used was a 19-item questionnaire which included age, gender, and relevant GI symptoms. Patients took no more than 5 min to answer all questions. This questionnaire was developed through review of the literature, and similar instruments as well as discussions among study investigators.

The Epi-Info version 6 was used to calculate the sample size. A sample size of 95 cases and 95 controls was computed based on a confidence level of 95%, power of 80%, and a 1:1

ratio for cases and controls. The sample was inflated to 100 individuals per group to account for an estimated non-response rate of 5%. Data entry and analysis were carried out using SPSS Version 12.0 for Windows. Descriptive characteristics of the data were summarized by generating measures of central tendencies and variability as appropriate for the types of variables. Inferential analysis of the data included use the Chi-square and t test.

Results

From August 2009 to June 2010, 99 consecutive HIV patients (study patients) and 97 consecutive blood donors (control group) were evaluated.

All participants from the CHARES clinic had documented HIV seropositivity as determined by enzyme-linked immunosorbent assay (ELISA), and confirmed by Western blot. In the HIV group there were 55 females and 44 males, compared to 63 males and 34 females in the control group. The majority of patients were between the ages of 36-60 years of age (31% of males, 33% of females) as compared to the control group in which the majority of participants were between the ages of 18-35 years (45% of males, 24% of females) ($p < 0.004$).

Of the fourteen GI symptoms evaluated by the research questionnaire, data were available for 196 respondents and the profile of these GI symptoms is shown in Table 1. Of the symptoms evaluated, those found to be relatively uncommon to both study groups were anorexia, dysphagia, odynophagia and vomiting. Among HIV patients, the mean number of symptoms was 2.9 (range 0-11, SD 2.2; 95% Confidence Interval 2.4-3.3). Among the controls, the mean number of symptoms was 3.3, (range 0-10; SD 2.1; 95% Confidence Interval 2.8-3.7). There was no significant difference in the average number of symptoms between the two groups ($p = 0.091$).

Weight loss within the past year was present in 37.4% of the HIV patients and 35.1% of the control group. The majority of persons in both groups had experienced weight loss of up to twenty pounds.

Dysphagia and odynophagia were present in 8.1% of HIV patients and 3.1% of the controls ($p = 0.129$). Only one HIV participant had experienced dysphagia for 10 months. Additionally, 1 HIV participant experienced odynophagia for 6 months.

Abdominal bloating was noted in 15.2% of HIV patients and 20.6% of the control participants. For both groups, bloating episodes were relatively frequent, with the majority of persons reporting an occurrence of about once a month. Among the HIV patients, 4 persons noted that their bloating had lasted longer than 5 years. Belching was present in 59.6% of HIV patients and in 96.8% of controls ($p < 0.001$). In the control group, 44.3% had heartburn compared to 29.3% of HIV patients.

Within the preceding 12 months, 26.3% of HIV participants and 12.4% of the control group reported having sought medical attention for their GI symptoms ($p = 0.001$). Of this

Table 1 Gastrointestinal symptoms

| | HIV Patients (N =99) | | Controls (N = 97) | | Fisher's Exact P value |
|----------------------------|-------------------------|-------|----------------------|-------|---------------------------|
| | Number | % | Number | % | |
| Appetite: | | | | | |
| Normal | 66 | 66.7% | 78 | 80.4% | 0.062 |
| Increased | 22 | 22.2% | 10 | 10.3% | |
| Decreased | 11 | 11.1% | 9 | 9.3% | |
| Weight Loss | 37 | 37.4% | 34 | 35.1% | 0.768 |
| Difficulty Swallowing | 5 | 5.1% | 3 | 3.1% | 0.721 |
| Pain Swallowing | 4 | 4.0% | 0 | --- | 0.121 |
| Abdominal Bloating | 15 | 15.2% | 20 | 20.6% | 0.355 |
| Early Satiety | 29 | 29.3% | 14 | 14.4% | 0.015* |
| Belching | 59 | 59.6% | 91 | 96.8% | <0.001* |
| Heartburn | 29 | 29.3% | 43 | 44.3% | 0.038* |
| Nausea | 21 | 21.2% | 34 | 35.4% | 0.038* |
| Vomiting | 6 | 6.1% | 3 | 3.1% | 0.498 |
| Upper Abdominal Discomfort | 12 | 12.1% | 11 | 11.3% | 1.000 |
| Lower Abdominal Discomfort | 15 | 15.2% | 18 | 18.6% | 0.570 |
| Diarrhea | 18 | 18.2% | 17 | 17.5% | 1.000 |
| Rectal Bleeding | 25 | 25.3% | 14 | 14.4% | 0.073 |

subset of HIV patients, 12.12% had sought medical attention as frequently as once per month. Only 8% of HIV patients and 12.4% of controls had their symptoms investigated by a physician ($p=0.354$). However, 95% of HIV patients and 90% of the control group reported that none of their GI symptoms had significantly affected their quality of life ($p=0.067$).

At the time of the interview, 89 of HIV patients had recent CD4 counts available. Sixty seven percent of these patients had CD4 counts greater than 350 cells/ μL , with a mean CD4 count of 472 cells/ μL .

Eighty five percent of the HIV patients were on antiretroviral treatment and had a mean CD4 count of 460.5 cells/ μL (SD 346.4). The treatment naïve subset (15%) had a mean CD4 count of 554.3 cells/ μL (SD 263.3). In this latter group, the most common symptoms were weight loss, early satiety and belching. However, there were no significant differences in GI symptoms between the treatment naïve subset and those on antiretrovirals. The presence of GI symptomatology according to immune status in the HIV group were as follows; patients with a CD4 count of less than 200 cells/ μL ($n=14$) reported as many as 6 of the 14 GI symptoms asked, those with CD4 of 201-350 cells/ μL had 3 symptoms compared to patients with CD4 counts greater than 351 cells/ μL who had only one symptom. Significantly more patients with CD4 counts greater than 500 cells/ μL had normal appetite than those with CD4 counts less than 350 cells/ μL ($p=0.034$). In addition,

belching was significantly more common in the latter group than in patients with CD4 greater than 500 cells/ μL ($p=0.040$). Pain on swallowing, and vomiting were significantly more common in patients with CD4 <350 cells/ μL than in controls (Table 2). However, significantly more control patients had normal appetite and belching than HIV patients with CD4 < 350 cells/ μL .

Discussion

Upper and lower GI symptoms are common in the general population and are associated with decreased quality of life [8]. In Jamaica and the Caribbean no prior study has been performed on the prevalence of common GI symptoms. In addition, there has not been any study published on patients with HIV on the prevalence of GI symptoms which may significantly affect the quality of life of these patients. In general, appropriate symptom management requires improved symptom recognition and should be an essential component of patient care at all stages of any disease [9]. In the present study, GI symptoms were common in ambulatory HIV patients and controls with 26.3% of HIV patients and 12.4% of controls having to seek medical attention for GI related symptoms and about 50% had to seek help monthly.

Table 2 Symptoms in patients with CD4 < 350 cells/ μ L and controls

| | CD4 < 350 (N = 28) | | Controls (N = 97) | | Fisher's Exact p-value |
|----------------------------|-----------------------|------|----------------------|------|---------------------------|
| | Number | % | Number | % | |
| Appetite: | | | | | |
| Normal | 16 | 57.1 | 78 | 80.4 | 0.037* |
| Increased | 6 | 21.4 | 10 | 10.3 | |
| Decreased | 6 | 21.4 | 9 | 9.3 | |
| Weight Loss | 10 | 35.7 | 34 | 35.1 | 1.000 |
| Difficulty Swallowing | 2 | 7.1 | 3 | 3.1 | 0.312 |
| Pain Swallowing | 2 | 7.1 | 0 | --- | 0.049* |
| Abdominal Bloating | 4 | 14.8 | 20 | 20.6 | 0.592 |
| Early Satiety | 8 | 28.6 | 14 | 14.4 | 0.096** |
| Belching | 21 | 75.0 | 91 | 96.8 | 0.001* |
| Experience Heartburn | 8 | 28.6 | 43 | 44.3 | 0.190 |
| Nauseous | 6 | 21.4 | 34 | 35.4 | 0.250 |
| Vomiting | 4 | 14.3 | 3 | 3.1 | 0.044* |
| Upper Abdominal Discomfort | 2 | 7.1 | 11 | 11.3 | 0.731 |
| Lower Abdominal Discomfort | 4 | 14.3 | 18 | 18.6 | 0.780 |
| Diarrhea | 8 | 28.6 | 17 | 17.5 | 0.282 |
| Rectal Bleeding | 8 | 28.6 | 14 | 14.4 | 0.096** |

*significant ($p < 0.05$); ** borderline significant ($0.05 \leq p < 0.10$)

The occurrence of dysphagia in 8.1% of patients with HIV in the present study is slightly more than that reported in a previous study in ambulatory patients of 5% [10]. Odynophagia was present only in the HIV patients and not in the control group in this study. In HIV patients with advanced immunodeficiency with CD4 counts of less than 200, infection of the esophagus is the most common cause of dysphagia [6]. In fact, the commonest cause of esophageal symptoms is candidiasis, followed by cytomegalovirus infection which produces either diffuse esophagitis or discrete ulcerations [11].

Gastro-esophageal reflux manifests as a continuum of symptom frequency and/or severity in the general population. An approximate prevalence of 10–20% was identified for gastro-esophageal reflux disease, defined by at least weekly heartburn and/or acid regurgitation in the Western world, while in Asia this was lower, at less than 5% [12]. In the present study 44% of controls and 29% of HIV patients had heartburn. It is of interest that belching was the most common symptom in both groups of our study and was the only symptom which was present significantly more in the control group. Belching is usually due to air swallowing. In the upright position ingested air will accumulate in the proximal stomach and the resulting distention elicits transient relaxation of the lower esophageal sphincter, allowing the ingested air to be vented [13,14]. Belching is a common symptom in patients with gastro-esophageal reflux disease and functional dyspepsia [14,15].

Weight loss is a common feature of late HIV infection

[11]. Weight loss was present in 37.4% of HIV patients in the present study which is similar to a recent study in which weight loss was present in 34% [16]. In another study, 37% of HIV patients had developed weight loss by 36 months [10]. The incidence of the HIV wasting syndrome has fallen dramatically in the era of successful antiviral therapy. However, weight loss and wasting still occur and are associated with significant morbidity and increased mortality. In patients with AIDS, the mechanism(s) of wasting is multifactorial including reduction in nutritional intake, anorexia, medications and GI diseases which are frequently infectious and often cause diarrhea [6,17]. It is however, surprising that 35% of control patients had weight loss. Weight loss as reported in this study is subjective and this perception may be inaccurate. In addition, the questionnaire did not seek to determine if weight loss was intentional.

GI complications have fallen substantially with antiviral treatment. Advances in antiretroviral therapy are changing the nature of HIV disease and affecting many of the GI manifestations [17]. The prevalence of opportunistic diseases has decreased significantly while the prevalence of gastro-esophageal reflux disease has increased [6]. In the current study the presence and number of symptoms were directly associated with the CD4 count. Patients with lower counts had more symptoms compared with those with higher counts [18]. Also, patients with lower CD4 count are more likely to develop GI symptoms [10]. In addition, patients with a CD4 count less

Summary Box

What is already known:

- The gastrointestinal (GI) tract is a common site of involvement in HIV infection
- These GI manifestations may be debilitating
- Opportunistic infections, neoplasms, inflammatory changes and direct mucosal invasion of the gastrointestinal tract by HIV, are well recognized causative factors

What the new findings are:

- GI symptoms are common in ambulatory HIV patients and controls
- In HIV patients the presence of symptoms was directly related to CD4 count
- HIV patients frequently sought medical attention for their GI symptoms
- Early satiety was the only symptom significantly more common in the HIV patients
- The improved GI outcome in HIV patients reflect the changing manifestations of HIV infection which may due to the success of antiretroviral therapy

than 200 cells/ μ L are those at highest risk for opportunistic infections and the risk of disease rises exponentially with a fall in CD4 count to less than 100 cells/ μ L [6,18].

There were limitations to the present study. The sample of HIV patients is not entirely representative of the general population of HIV patients but represent only the ambulatory patients, which nonetheless constitute the majority of HIV patients. Also, the number of patients and controls was relatively small.

In conclusion, the present study revealed that GI symptoms were common in ambulatory HIV patients and controls. In HIV patients the presence of symptoms was directly related to CD4 count. Early satiety was the only symptom significantly more common in the general HIV patients, while heartburn, belching and nausea were more common in the control patients. However, pain on swallowing, and vomiting were significantly more common in patients with CD4 <350 cells/ μ L than in controls. The relatively low incidence of significant GI symptoms in HIV patients may reflect the changing manifestations of HIV infection due to the success of antiretroviral therapy.

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Appendix

Prevalence of upper and lower gastrointestinal symptoms

Questionnaire

1. What is your age in years?
 1. 20 - 24
 2. 25 - 30
 3. 31 - 35
 4. 36 - 40
 5. 41 - 45
 6. 46 - 50
 7. 51 - 60
2. Please indicate your gender
 1. Male
 2. Female
3. How would you describe your appetite within the last year?
 1. Normal
 2. Increased
 3. Decreased
4. Have you lost weight in the past year?
 1. Yes
 2. No

If yes, please quantify how much weight you may have lost within the past year

 1. None
 2. 5-10 lbs
 3. 10-20 lbs
 4. 20-30 lbs
 5. >30 lbs
 6. Do not know how much
5. Do you experience any difficulty when swallowing?
 1. Yes
 2. No

If yes how long?
6. Do you experience any pain when swallowing?
 1. Yes
 2. No

If yes how long?
7. Do you experience any abdominal bloating?
 1. Yes
 2. No

If yes how long?

 1. Every Day or More
 2. 2-6 Times a Week
 3. About Once a Week
 4. About Once a Month
 5. Never
8. Do you experience early satiety (easily full after a small meal)?
 1. Yes
 2. No

If yes how long?
9. How often do you belch?
 1. Every Day or More
 2. 2-6 Times a Week
 3. About Once a Week
 4. About Once a Month
 5. Never
10. Do you ever experience heartburn (i.e. burning in the middle of the chest or sensation of acid rising to the back of the throat)?
 1. Yes
 2. No

If yes how long?

How often?

 1. Every Day or More
 2. 2-6 Times a Week
 3. About Once a Week
 4. About Once a Month
 5. Never
11. How often do you feel nauseous (sensation to vomit)?
 1. Every Day or More
 2. 2-6 Times a Week
 3. About Once a Week
 4. About Once a Month
 5. Never
12. Do you suffer from vomiting?
 1. Yes
 2. No

If yes how long?

How often?

 1. Every Day or More
 2. 2-6 Times a Week
 3. About Once a Week
 4. About Once a Month
 5. Never
13. Do you experience upper abdominal discomfort (i.e. above the level of the navel)?
 1. Yes
 2. No

If yes how long?

How often?

 1. Every Day or More
 2. 2-6 Times a Week
 3. About Once a Week
 4. About Once a Month
 5. Never
14. Do you experience lower abdominal pain (i.e. below the level of the navel)?
 1. Yes
 2. No

If yes how long?

How often?

 1. Every Day or More
 2. 2-6 Times a Week
 3. About Once a Week
 4. About Once a Month
 5. Never
15. Do you experience diarrhea (i.e. frequent, soft or watery feces)?
 1. Yes
 2. No

If yes how long?

How often?

 1. Every Day or More
 2. 2-6 Times a Week
 3. About Once a Week
 4. About Once a Month
 5. Never
16. Have you ever had bleeding from the rectum or noticed blood on passing stools?
 1. Yes
 2. No

If yes how long?

How often?

 1. Every Day or More
 2. Times a Week
 3. About Once a Week
 4. About Once a Month
 5. Never
17. During the past 12 months, how many times have you had to seek medical attention for the above symptoms?
 1. Never
 2. Once per year
 3. Every other month
 4. Once a month
18. Have you ever had your symptoms investigated by your doctor?
 1. Yes
 2. No
19. To what extent do these symptoms affect your quality of life or activities of daily living?
 1. Every Day or More
 2. About Once a Week
 3. About Once a Month
 4. Never