ORIGINAL RESEARCH PAPER

Volume-8 | Issue-3 | March-2019 | PRINT ISSN No 2277 - 8179

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

ENDOSCOPIC FINDINGS IN PATIENTS WITH HUMAN IMMUNODEFICIENCY VIRUS

Medicine

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ABSTRACT

Introduction: The gastrointestinal tract is a major source of disease in patients with human immunodeficiency virus. In addition to opportunistic infections, immunosuppression also predisposes patients to neoplasias, with Kaposi's sarcoma being the most common.

Objective: To describe the frequency of various endoscopic findings in patients with HIV and determine whether they are associated with viral load, CD4+ cell count and use of antiretroviral therapy.

Material and Methods: A retrospective study was performed using medical records of HIV-positive patients treated at the Doctor Heitor Vieira Dourado Tropical Medicine Foundation from January to August 2017. Data were collected on gender, age, diagnosis time, antiretroviral use, CD4+ T cell count, viral load and the endoscopic findings of each patient. The data were analyzed and reported as descriptive statistics.

Results: The most frequent endoscopic finding was Helicobacter pylori, although a relationship between the presence of this bacterium and HIV infection was not established. Candida esophagitis was the second most frequent finding, with cytomegalovirus and herpetic esophagitis identified as well. Other opportunistic infections coincident with immunosuppression and low CD4+ cell count were also identified, such as hookworm, cryptosporidiosis and histoplasmosis. Six neoplasms were identified, with three being classified as Kaposi's sarcoma, which is a very common type of cancer in immunosuppressed individuals.

Conclusion: The most common endoscopic findings were Helicobacter pylori and candida esophagitis. These, as well as other opportunistic diseases diagnosed, were found more frequently in patients with increased viral load and CD4+ T cell counts less than 200 cells/mm3. Endoscopy is important for the early diagnosis of these pathologies and may reduce secondary complications and thus reduce the morbidity and mortality of these patients.

KEYWORDS

Endoscopy. Human immunodeficiency syndrome. Human immunodeficiency virus.

INTRODUCTION

The gastrointestinal tract (GIT) is an important source of disease in patients with human immunodeficiency virus (HIV). More than half of HIV-infected patients have symptoms related to the GIT, and most develop related complications. The most commonly reported symptoms are anorexia, weight loss, dysphagia, odynophagia, abdominal pain and diarrhea, which although quite frequent, are not specific to these patients [1,2].

Over the past three decades, studies have identified a variety of inflammatory, infectious and neoplastic diseases associated with HIV, which often have a specific predilection for some sites of the GIT. The esophagus is one of the main target organs for both opportunistic infections and neoplasms. Approximately one-third of patients with Acquired immunodeficiency syndrome (AIDS) will develop esophageal symptoms at some point in the course of the disease. In addition, the development of opportunistic esophagitis may be a predictive factor of worse long-term prognosis, reflecting the underlying severe immunodeficiency [3,4]. Esophageal diseases associated with HIV include candidiasis, cytomegalovirus (CMV) infections, herpes simplex virus (HSV) infections and idiopathic ulceration. Gastric disease, although less common than esophageal disease, often involves CMV, Mycobacterium avium-intracellulare (MAI) and neoplasms Kaposi's sarcoma (KS) and lymphoma. Colorectal biopsies commonly demonstrate viral (CMV, HSV), bacterial (Clostridia, Salmonella, Shigella, Campylobacter), fungal (cryptococcosis, histoplasmosis) and neoplastic (KS, lymphoma) processes [1].

However, the availability of highly active antiretroviral therapy (ART) improves not only the patient's systemic immunity but also the cellular immunity associated with the GIT, drastically reducing these associated illnesses [5,6]. According to Crum-Cianflone, CD4+ T cell count below 100-200 cells/mm^3 increases the risk of opportunistic infections caused by viral, bacterial, fungal and parasitic pathogens, which highlights the importance of ART adherence [2].

Regarding the identification of many of the aforementioned comorbidities, upper gastrointestinal endoscopy is the diagnostic test of choice because it is a sensitive, specific and low-risk method. It allows endoscopic and histopathological evaluation of samples from the upper portion of the GIT, making it possible to diagnose patients with non-specific symptoms or who are asymptomatic [1,7].

Thus, identification and treatment of gastrointestinal (GI) changes may be crucial in reducing cases of neoplasia and other changes that affect the nutritional status of these patients, which may aggravate or favor the manifestation of AIDS symptoms [8,9]. Thus, the present study aimed to describe the frequency of endoscopic findings in HIV patients and determine whether they are related to viral load, CD4+ T cell count and use of antiretroviral therapy.

MATERIALS AND METHODS

Characterization of the study, sample and institution

This is a retrospective study using the medical records of HIV-positive patients treated at the Doctor Heitor Vieira Dourado Tropical Medicine Foundation (FMTHVD) from January to August 2017.

FMTHVD is an important tertiary center for the treatment of infectious diseases in Manaus (State of Amazonas - Brazil); it is seen as an example of excellent care and follow-up of patients with HIV/AIDS, and it has an outpatient clinic, emergency room, forty hospital beds and seven beds in the intensive care unit (ICU). The FMTHVD is the only unit of the public health network in the city of Manaus that admits patients with HIV/AIDS. The foundation also has a pathology service, where histological analyses are performed.

Data collection and analysis

Patients' records were reviewed and the following information was collected: gender, age, time of disease diagnosis, antiretroviral use, CD4+ T cell count, viral load and endoscopic findings.

The endoscopies were performed by accredited medicals experts at the Foundation's digestive endoscopy service using a Pentax EPK-1000 processor and Pentax EG-2770K gastroscope.

Data were analyzed and reported as descriptive statistics (absolute and relative frequency), and the means, standard deviations (SD) and medians were calculated for age, CD4+ T cell count and viral load. In addition, to test for possible relationships between endoscopic findings and the course of the disease (AIDS/HIV), endoscopic findings were presented according to their frequency in individuals with a CD4+ T cell count < 200 cells/mm^3, who according to the literature are at the highest risk for HIV-related complications [9].

Tests that resulted in undetectable viral load were counted and considered to be zero.

RESULTS

Characterization of the sample

Between January and August 2017, 151 endoscopies were performed in patients with AIDS/HIV, and 75 patients (49.66%) exhibited a total of ninety relevant endoscopic findings.

Sixty (80%) endoscopic findings were from male patients, and the mean age ± SD of the sample was 40.13 ± 11.34 years, with a median of forty years.

There was a large range in the months since HIV diagnosis. Some patients were previously unaware their diagnosis, and some had been living with the disease for years. The mean time since diagnosis was 61.83 ± 60.17 months, with a median of 48 months.

The use of ART was evaluated only in terms of follow-up, and 80% of patients with relevant endoscopic findings were being treated. The mean ± SD CD4+ T cell count and viral load were 210.19 ± 292.62 cells/mm^3 (median of 50 cells/mm^3) and 211,459 ± 356,818 copies/mL (median of 31,096 copies/mL), respectively.

Among the 90 (100%) relevant endoscopic findings, the most frequent were Helicobacter pylori colonization in 58 (64.45%) and esophageal candidiasis in 17 (18.9%). Other findings included CMV esophagitis (2 findings, 2.22%), intestinal hookworms (2 findings, 2.22%), KS (3 findings, 3.33%), cryptosporidiosis (2 findings, 2.22%), herpetic esophagitis (1 finding, 1.11%), histoplasmosis (2 findings, 2.22%), moderately differentiated adenocarcinoma of the esophagus (1 finding, 1.11%), moderately differentiated tubular gastric adenocarcinoma (1 finding, 1.11%) and undifferentiated large cell neoplasia - CD30 and CD45RB (1 finding, 1.11%).

Images of each of the findings, with the exception of H. pylori, are shown in Figure 1.

Characterization of the sample

In the following figures, the endoscopic findings are shown by gender (Figure 2A), CD4+ T cell count (Figure 2B), time since diagnosis (Figure 2C) and use of ART (Figure 2D).

The frequency of endoscopic findings in patients with CD4+ T cell counts below 200 cells/mm^3, viral load and use of ART were also evaluated.

DISCUSSION

HIV is a virus with a preferential tropism for CD4+ T cells, also known as helper T lymphocytes, which are responsible for coordinating various functions of acquired immunity. They recruit the help of innate immunity in order to promote greater efficacy of elimination of diverse pathogens, as well as in the generation of memory after contact with an antigen. Thus, when such cells are destroyed by HIV, there are systemic repercussions on the immune response, which is shown to be prone to so-called opportunistic infections, such as candidiasis, endoparasites and viroses [10].

Many of our patients were men in the fourth decade of life, which is consistent with data presented by Sá et al. [11]. These authors reported a mean CD4+ T cell count of 289 cells/mm^3 and mean viral load of 316.000 copies/mL in males [11]. Although in the present study we did not stratify these findings by gender, our results are similar.

The relationship between HIV and the most common endoscopic finding in our study, H. pylori, remains controversial; while H. pylori is transmitted by gastro-fecal-oral routes and is associated with low socioeconomic status, HIV is transmitted through sexual intercourse, infected body fluids and transplacentally. If the host responses to these infections were independent, the prevalence of H. pylori should be similar in HIV-infected and uninfected patients. However, several studies have detected a lower prevalence of H. pylori in patients with HIV infection, while other studies found no differences or higher rates of H. pylori in HIV-positive individuals [12]. Therefore, the high frequency with which this infection was found in the sample may be more related to the socioeconomic conditions of the study sample than to HIV infection. While we did not investigate the socioeconomic characteristics of our patients, Manaus is one of the five Brazilian cities with the greatest social inequality, with 35% of its population characterized as low income and 17% characterized as poor. In addition, more than 30% of households do not have basic sanitation, favoring the acquisition of infections transmitted by fecal-oral routes [13].

The other alterations identified by upper digestive endoscopy, with the exception of adenocarcinoma and large cell neoplasia, can be considered opportunistic infections, which are frequent in HIV-positive patients in Latin America [13,14]. According to Okeke et al. [15], 35% of patients with HIV/AIDS in Nigeria developed esophageal candidiasis. The difference found between the data presented here and the study by Okeke et al. [15] can be explained by the greater difficulty accessing antiretroviral therapy in Nigeria.

The two cases of adenocarcinoma can be explained by the fact that the risk of neoplasia in HIV-infected persons is high and estimated to be twice the risk of the general population [16,17].

As already mentioned, the GIT is directly affected by HIV infection, as it is the largest lymphoid organ in the human body. HIV damages the intestinal cells, resulting in flattening of villi and decreased absorption of D-xylose. This leads to a poor absorption of carbohydrates and fats, affecting the fat-soluble vitamins such as vitamins A and E, which are important for proper functioning of the immune system. Therefore, because these events in the GIT are more frequent in patients with HIV/AIDS, they may contribute to poor nutritional status in these individuals or even to the development of neoplasias [18].

One factor responsible for malnutrition in HIV-infected individuals is reduced appetite, which may be due to difficulty eating. This can result from infections such as oral thrush and esophagitis, which may be caused by Candida, drug side effects or depression. Another factor is the malabsorption of nutrients, whose main causes include alteration in the villus architecture, as described above; diarrhea due to bacterial infections such as Salmonella or Mycobacterium avium; viral diarrhea such as CMV; and parasitic infections such as those caused by Giardia and others. In developed countries, 30-50% of patients with HIV experience diarrhea and malabsorption, while in developing countries, this proportion reaches 90% [19,20].

This corroborates the endoscopic findings reported in this study because the high rate of H. pylori may be associated with the appearance of gastric lesions accompanied by pain and hemorrhage; esophagitis (either from candida, herpes virus or CMV) with dysphagia and anorexia; and intestinal parasites, with diarrhea, anemia and malabsorption of nutrients. This underscores the primary importance of identifying these alterations, as they can lead to worsening of the patient's general state [20].

Analysis of the endoscopic findings revealed a relationship between some changes and low CD4+ T cell counts and increased viral load.

Among patients with H. pylori and esophageal candidiasis, 55.17% and 82.35%, respectively, had CD4+ T cell counts less than 200 cells/mm^3, and the viral load in these patients was increased by an average of 80.000 copies/mL compared to patients with higher CD4+ T cell counts. There were no significant relationships between the other endoscopic findings and either low CD4+ T cell count or viral load, which can be attributed to small sample size.

The absence of antiretroviral treatment was not associated with these variables, as many patients who reported being treated had a low CD4+ T cell count and elevated viral load. However, this deserves investigation because what initially appears to be ART failure may actually be low adherence, which in the study population of Silva et al. [21] was reported to be 25%.

Other findings that were less frequent in this study are diseases known to have a higher incidence in AIDS patients. Cryptosporidiosis, for example, is an infection caused by the protozoan of the genus *Cryptosporidium* spp., which infects human and animal GI epithelial cells [22]. The clinical manifestations depend on the immune status of the patient, and in patients with AIDS and advanced immunodeficiency, it is the most common parasitic cause of prolonged diarrhea associated with severe weight loss, which may lead to severe dehydration and electrolyte disturbance [22,23]. This was observed in two patients whose mean CD4+ T cell count was markedly low (17.5 ± 7.8 cells/mm^3).

Likewise, despite the high prevalence of endoparasitic diseases in Brazil being considered a public health issue, intestinal hookworms were found in only two patients. In immunosuppressed patients, such as the sample in question, the risk of parasitic infection is considerably higher, and immunodepression not only provides greater susceptibility to contamination by opportunistic agents but also more severe symptomatology [24]. Histoplasmosis, a fungal infection, can also cause serious manifestations due to its spread in immunosuppressed patients and was identified in two of our patients.

This state of immunosuppression, as previously mentioned, also predisposes patients to the appearance of neoplasia's, which were observed in six patients. KS is the most incident and prevalent cancer in individuals with HIV/AIDS, and this was also found in the present study. KS can occur in up to the six following forms of clinical presentation: macular, plaque, nodular, exophytic, infiltrative and lymphadenopathic. KS lesions are highly angiogenic and, as a result, are usually red, purple, or brown in color [25]. KS lesions are predominant in the skin, which is the most affected organ, with pulmonary and digestive manifestations being the next most common. KS mortality is associated with opportunistic infections, gastrointestinal bleeding and pulmonary complications [26,27].

The main endoscopic findings in this study were H. pylori infection and esophageal candidiasis, which represented approximately 80% of the alterations found. Although H. pylori is not a finding specific to patients with HIV/AIDS, many patients were found to be affected (64%).

It is also possible to infer a relationship between these findings and low CD4+ T cell count, as more than half of patients with H. pylori and more than 80% of patients with esophageal candidiasis had a CD4+ T cell count less than 200 cells/mm^3. It was also found that the viral load was increased by an average of 80.000 copies/mL in patients with low cell count.

The absence of ART was not directly related to CD4+ T cell count and viral load.

Half of the patients in this sample suffered some endoscopic alteration, confirming that endoscopic follow-up is of paramount importance in this population for the early identification and prevention of secondary complications that increase the risk of morbidity and mortality.

There is no conflict of interest

Table 1. Demographic and clinical characteristics of patients positive for the HIV rapid test and who underwent upper digestive endoscopy

Feature		Number of Patients
Characteristics		
Gender	Male Female	60 (80%) 30 (20%)
Age (years)	Mean ± SD Median	40.13 ± 11.34 40
Clinical findings		
Antiretroviral treatment	Yes No	60 (80%) 30 (20%)
CD4+ T Cell Count	Mean ± SD Median	210,19 ± 292,62 cells/mm^3 50 cells/mm^3
Viral load	Mean ± SD Median	211,459 ± 356,818 copies/mL 31,096 copies/mL
Endoscopic findings	Helicobacter pylori Esophageal candidiasis CMV esophagitis Intestinal hookworms Cryptosporidiosis Kaposi's sarcoma Herpetic esophagitis Histoplasmosis Moderately differentiated adenocarcinoma of the esophagus Moderately differentiated tubular gastric adenocarcinoma Undifferentiated large cell neoplasm	58 (64.45%) 17 (18.90%) 2 (2.22%) 2 (2.22%) 2 (2.22%) 3 (3.33%) 1 (1.11%) 2 (2.22%) 1 (1.11%) 1 (1.11%) 1 (1.11%)

Table 2. Endoscopic findings related to immunological condition, viral load and adherence to antiretroviral therapy

Endoscopic Finding	Patients with CD4+ T cell count < 200 cells/ mm^3	Viral load (copies/mL)	Denies use of Art
Helicobacter pylori	32 (35.5%)	212,314 ± 361,626	14
Esophageal candidiasis	40.65 ± 43.96 14 (15.5%)	186,994 ± 272,666	8
CMV Esophagitis	20.35 ± 13.76 2 (2.2%)	268,279 ± 378,965	1
Intestinal hookworms	35.5 ± 4.95 1 (1.1%)	Not detected	1
Kaposi's sarcoma	21 3 (3.3%)	693,621 ± 827,300	0
Cryptosporidiosis	119.3 ± 60.7 2 (2.2%)	39,133 ± 51,058	0
Herpetic esophagitis	17.5 ± 7.8 1 (1.1%)	604,010	1
Histoplasmosis	28 2 (2.2%)	98,587 ± 139,423	0
Adenocarcinoma of the esophagus	47.5 ± 51.6 1 (1.1%)	1094	1
Undifferentiated large cell neoplasm	195 0	41988	0

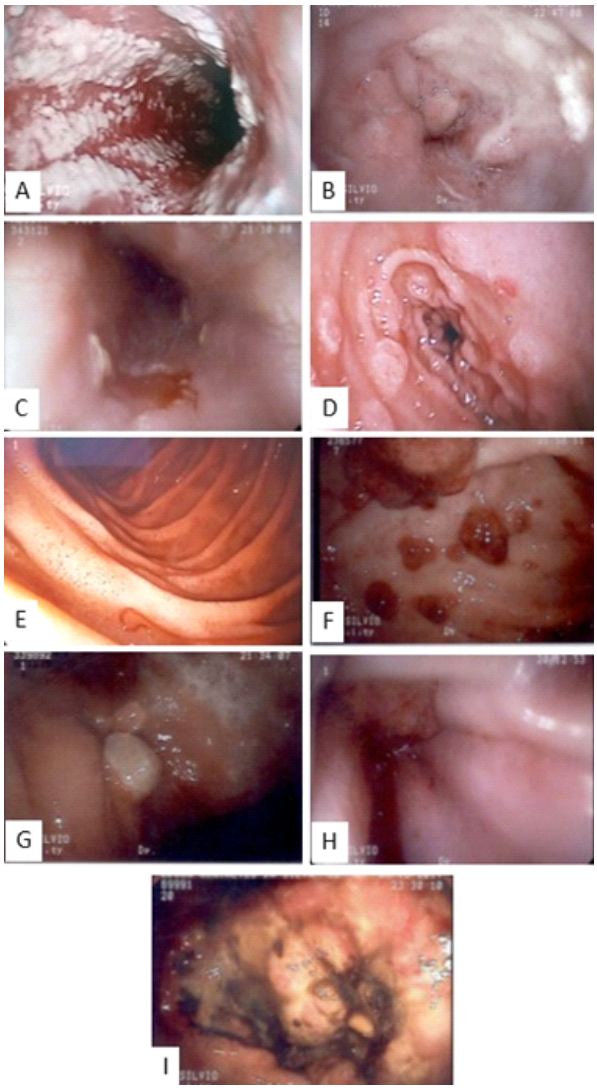

Figure 1. Representative image of relevant endoscopic findings in patients with HIV: A) Esophageal candidiasis; B) Cytomegalovirus infection; C) Herpetic esophagitis and candida esophagitis; D) Histoplasmosis; E) Endoparasite infection. F) Kaposi's sarcoma; G) Undifferentiated hematopoietic neoplasm of large cells; H) Moderately differentiated adenocarcinoma of the esophagus; I) Moderately differentiated tubular gastric adenocarcinoma.

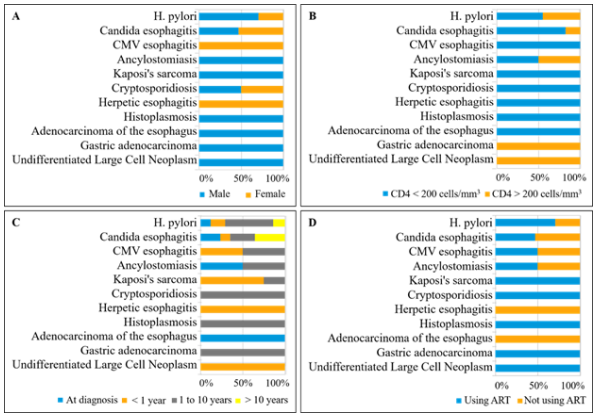

Figure 2. Distribution of patients according to endoscopic findings and the following characteristics: A) Gender; B) CD4+ T cell count; C) Time since diagnosis; D) Use of antiretroviral therapy (ART).

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