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Editorial

The Challenge of Evaluation of Gastrointestinal Symptoms in HIV Patients

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HIV disease is a frequent infection, whose number of individuals living with it worldwide exceeds 37 million [1]. Among the lots of complications which it causes are gastrointestinal and hepatobiliary disorders [2]. More than 50% of all HIV patients had reported gastrointestinal (GI) symptoms during their disease [3,4].

HIV and gastrointestinal system appears to have a relation. The gastrointestinal tract has a primary role in pathogenesis of HIV infection [5]. Studies have shown that GI system is a main site of HIV replication and CD4 T-cell death [6]. During the infection there is considerable reduction of CD4 T-cells within the gut-associated lymphoid tissue (GALT) [7].

Some of the GI symptoms of HIV disease include diarrhea, dysphagia and odynophagia, nausea, vomiting, weight loss, abdominal pain and GI bleeding [2]. Most common GI manifestation in outpatients is diarrhea with prevalence 0.9 – 14%, while the prevalence in inpatients reaches the 50% [8,9].

Diarrhea, the most common GI complaint, can occur during both acute HIV infection and advanced disease. Causes of diarrhea in these patients can be divided in four groups: infections, medications, neoplasms and idiopathic. A broad variety of pathogens has implicated, like protozoa, viruses, bacteria and funguses. More frequent causes are *Cryptosporidium, Microsporidium, Mycobacterium avium-complex* (MAC), *Salmonella, Shigella* and *Cytomegalovirus* (CMV) [2]. Some pathogens, such as MAC and CMV, infect only HIV patients with CD4 cell count < 100/mm^3, while others, like *Cryptosporidium*, cause diarrhea in healthy immunocompetent hosts [10-12]. The diarrhea caused by medications (including protease inhibitors, e.x Nelfinavir and Saquinavir) is often self-limited and lasting less than 2 to 4 weeks from initiation of medication administration [2]. Common GI neoplasms causing diarrhea is lymphoma and Kaposi's sarcoma [2]. Other etiologies of diarrhea include idiopathic colitis (AIDs enteropathy) [2].

AIDs enteropathy is defined as a chronic diarrheal disease with unknown etiology in patients of advanced stage of HIV disease [13]. Some data support that HIV itself acts as an indirect diarrheal pathogen altering the structure and function of the GI tract. As Kotler noted in 1984, in HIV patients were histological changes in the GI tract in the absence of other defined infectious or malignant etiologies [14]. The pathogenesis of HIV enteropathy is the result of negative affect of HIV at tubulin depolymerization and induction of local cytokines (e.g. interleukin IL-6, IL-10, tumor necrosis factor) causing altered epithelial ionic balances and enterocyte apoptosis [15-17]. These changes lead to mucosal atrophy and as a result there are as clinical features diarrhea and weight loss [18,19].

It is important to evaluate the symptom of diarrhea in patients with HIV disease in order to recognize treatable infections or neoplasms. Evaluation of diarrhea can be accomplished by obtaining a careful history including personal history (as lactose or food/fatty food intolerance), medications, and other indicative symptoms for systemic infection or neoplasm (as lymphadenopathy, hepatosplenomegaly) [2]. Stool must be examined for enteric bacteria, *Clostridium difficile* toxin, ova or parasite [2]. Sigmoidoscopy and biopsies are suitable if a diagnosis is not reached to identify CMV infection [2]. Colonoscopy is suggested for patients in whom sigmoidoscopy is nondiagnostic [2].

Patients of advanced HIV disease stage usually present involuntary weight loss [2]. This condition is due to various reasons. One cause is the calorie deficit because of anorexia, nausea, odynophagia and/ or dysphagia [2]. In addition, patients limit their oral intake in order to decrease symptoms of diarrhea, vomiting or abdominal pain [2]. Another possible etiology of malnutrition in HIV disease is the metabolic disturbance leading to increased energy consumption or irregular energy substrate usage due to opportunistic infections [2]. Therefore, there is need for extra caloric intake. A third reason of weight loss is the malabsorption due to intestinal mucosal disease, fast transit secondary to infectious diarrhea, pancreatic insufficiency or mucosal atrophy secondary to protein-calorie malnutrition [2]. Weight loss must be evaluated by a dietitian by monitoring changes in weight, body composition (body cell mass), caloric intake and activity [2].

Esophagitis is very common among patients with advanced HIV disease causing dysphagia and odynophagia [2]. The most frequent pathogen causing esophagitis to these patients is *Candida*. Other pathogens include *Cytomegalovirus* (CMV) and *Herpes Simplex Virus* (HSV). Except from infectious causes, odynophagia may be due to idiopathic ulceration, malignancies like Kaposi's sarcoma and lymphoma, and non-HIV-related disorders, such as acid-reflux esophagitis [2]. The CD4 levels can be used to manage the evaluation. *Candida* and HSV esophagitis are mainly identified in patients with CD4 cell levels less than 200 cells/mm^3, while CMV and idiopathic ulcers are mostly noted in patients with CD4 cell count less than 100 cells/mm^3 [2].

AAbdominal pain is ordinary in patients with HIV infection. During the evaluation of this symptom, a clinician besides the manifestations of opportunistic infections and neoplasms, must also examine the more common causes of abdominal pain in healthy persons [2]. The most frequent HIV-associated cause of abdominal pain is CMV infection of the bowel and biliary tract [2].

Although GI bleeding is rare showing up in less than 1% of patients with HIV disease, it may set difficult diagnostic and therapeutic challenges [2]. Besides the causes of GI bleeding occurring in healthy persons, for instance peptic or stress-related ulcer disease, inflammatory bowel disease, diverticular disease, colonic polyps, and neoplasia, there are also lesions unique to HIV [2]. More specifically, HIV-associated opportunistic infections can induce lesions by different mechanisms leading to GI bleeding. For example, CMV induces vasculitis in affected tissue, which results in ischemia and or infarction, usually in the colon or distal small bowel [20,21]. *Candida albicans* sometimes induces esophageal hemorrhage causing an intense erosive esophagitis [22]. In addition enteritis associated with *Salmonella, Shigella*, or *Campylobacter* is caused with increased incidence in HIV-infected patients. Moreover, HIV-associated neoplasms may cause intestinal bleeding, with the most common to be the Kaposi 's sarcoma [23].

GI bleeding in a patient with HIV disease should be assessed with the same approach used in evaluation of a non-HIV-infected patient. In order to define the source of the upper-tract bleeding, an upper endoscopy is essential, while a nuclear red blood cell scan is used to evaluate acute lower-tract hemorrhage, which is more useful than immediate colonoscopy.

There is no doubt that Highly Active Antitretroviral Therapy (HAART) contributes to a noteworthy reduction in morbidity and mortality related to HIV. On the one hand, studies have demonstrated that HAART improves the systemic immune system and the local cellular immunity of the GI tract [24]. As a result HAART improves some of the GI symptoms, such as HIV enteropathy [24]. Moreover, anti-HIV therapy in combination with chemoprophylaxis for pathogens who usually affect immunocompromised HIV patients (CD4 count lower than 200 cells/mm3), such as *Pneumocystis carinii, Mycobacterium avium, Cytomegalovirus*, can reduce the frequency of gastrointestinal opportunistic infections [2]. On the other hand, GI symptoms are among the short-term adverse effects of HAART, which are caused within a few months after the initiation of the therapy [25]. For instance, protease inhibitors can cause diarrhea [26].

Expanded life expectancy of HIV patients has as consequence the need of emphasis on chronic gastrointestinal disease and neoplasms. Intervention is necessary to recognize all reversible causes. As HIV disease becomes more a chronic condition, preservation of good nutrition status is an important goal to maintain the functional and energy capacity of individuals infected with HIV. We have to be aware that GI symptoms can impact the patients' life as well as medication adherence. People living with HIV disease and experiencing these symptoms tend to avoid social life due to adverse effects [27]. In conclusion, it is important to conduct researches focused on the appropriate treatment for HIV patients in order to improve their quality of life.

Bibliography

1. Global HIV and AIDS statistics — 2019 fact sheet. UNAIDS (2019).

2. Koch J., *et al*. "Gastrointestinal Manifestations of HIV". HIV In-Site Knowledge Base Chapter (1998).

3. Malenbranche R., *et al*. "Acquired immunodeficiency syndrome with severe gastrointestinal manifestations in Haiti". *Lancet* 2 (1983): 873-878.

4. Gazzard BG. "HIV disease and the gastroenterologist". *Gut* 29 (1988): 1497-1505.

5. Knox TA., *et al*. "Diarrhea and abnormalities of gastrointestinal function in a cohort of men and women with HIV infection". *The American Journal of Gastroenterology* 95 (2000): 3482-3489.

6. Nannini EC and Okhuysen PC. "HIV1 and the gut in the era of highly active antiretroviral therapy". *Current Gastroenterology Reports* 4 (2002): 392-398.

7. Veazey RS., *et al*. "Gastrointestinal tract as a major site of CD4+ T cell depletion and viral replication in SIV infection". *Science* 280 (1998): 427-431.

8. Wilcox CM., *et al*. "AGA Technical Review: Malnutrition and cachexia, chronic diarrhea, and hepatobiliary disease in patients with human immunodeficiency virus infection". *Gastroenterology* 111 (1996): 1724-1752.

9. Dworkin B., *et al*. "Gastrointestinal manifestations of the acquired immunodeficiency syndrome: A review of 22 cases". *The American Journal of Gastroenterology* 80 (1985): 774-778.

10. Gallant JE., *et al*. "Incidence and natural history of cytomegalovirus disease in patients with advanced human immunodeficiency virus disease treated with zidovudine". *Journal of Infection Disease* 166 (1992): 1223-1227.

11. Nightingale SD., *et al*. "Incidence of Mycobacterium avium-intracellulare complex bacteremia in human immune deficiency virus-positive patients". *Journal of Infection Disease* 165 (1992): 1082-1085.

12. Janoff EN and Smith PD. "Perspectives on gastrointestinal infections in AIDS". *Gastroenterology Clinics of North America* 17 (1988): 451-463.

13. Ulrich R., *et al*. "AIDS enteropathy". *Annals of Internal Medicine* 115 (1991): 328.

14. Kotler DP., *et al*. "Enteropathy associated with the acquired immunodeficiency syndrome". *Annals of Internal Medicine* 101 (1984): 421-428.

15. Kotler DP. "HIV infection and the gastrointestinal tract". *AIDS* 19 (2005): 107-117.

16. Maresca M., *et al*. "The virotoxin model of HIV-1 enteropathy: involvement of GPR15/Bob and galactosylceramide in the cytopathic effects induced by HIV-1 gp120 in the HT-29-D4 intestinal cell line". *Journal of Biomedical Science* 10 (2003): 156-166.

17. Schmitz H., *et al*. "Supernatants of HIV-infected immune cells affect the barrier function of human HT-29/B6 intestinal epithelial cells". *AIDS* 16 (2002): 983-991.

18. Ulrich R., *et al*. "Enteric immunologic abnormalities in human immunodeficiency virus infection". *Seminar on Liver Disease* 12 (1992): 167-174.

19. Riecken EO., *et al*. "Non-opportunistic causes of diarrhoea in HIV infection". In: Gazzard BG, ed. Bailliere's Clinical Gastroenterology. London: Balliere-Tindall 4 (1990): 385-403.

20. Foucar E., *et al*. "Colon ulceration in lethal cytomegalovirus infection". *American Journal of Clinical Pathology* 76 (1981): 788-801.

21. Meiselman MS., *et al*. "Cytomegalovirus colitis: Report of the clinical, endoscopic and pathologic findings in two patients with acquired immunodeficiency syndrome". *Gastroenterology* 88 (1985): 171-175.

22. Eras P., *et al*. "Candida infection of the gastrointestinal tract". *Medicine* 51 (1972): 367-379.

23. Cello JP and Wilcox CM. "Evaluation and treatment of gastrointestinal tract hemorrhage in patients with AIDS". *Gastroenterology Clinics of North America* 17 (1988): 639-648.

24. Kotler DP., *et al*. "Effect of combination antiretroviral therapy upon rectal mucosal HIV RNA burden and mononuclear cell apoptosis". *AIDS* 12 (1998): 597-604.

25. He M., *et al*. "Prospective observation for seven-year's highly active antiretroviral therapy in Chinese HIV-1 Infected patients". *Current HIV Research* 9 (2011): 160-165.

26. Wallace MR and Brann OS. "Gastrointestinal manifestations of HIV infection". *Current Gastroenterology Reports* 2 (2000): 283-293.

27. Tadesse WT., *et al*. "Self-reported adverse drug reactions and their influence on highly active antiretroviral therapy in HIV-infected patients: a cross-sectional study". *BMC Pharmacology and Toxicology* 15 (2014): 32.