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# Association of Gastrointestinal Manifestations with Socio-demographic, Lifestyle & Clinical Factors in HIV/AIDS Patients

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## Abstract

**Background**: Gastrointestinal abnormalities in people with HIV/AIDS have been reported since the advent of AIDS. This study aimed to analyze the gastrointestinal manifestations in HIV/AIDS patients in terms of sociodemographic, lifestyle, and clinical characteristics with the association of GI manifestations. **Material & Methods:** This observational cross-sectional analytical study was conducted at the ART corner and Department of Gastroenterology, Bangabandhu Sheikh Mujib Medical University, Shahbag, Dhaka among adult HIV-infected or AIDS patients aged more than 18 years. A total of 122 patients were taken as per inclusion criteria. The study took place from March 2018 to February 2019. Continuous variables were reported as the mean ± standard deviation. The correlation of several GI symptoms with CD4 count was done by the Spearman rank test. Sociodemographic variables (gender, age, income, and education level), lifestyle variables (smoking status, risk consumption of alcohol, and physical activity level), and clinical variables (antiretroviral therapy – duration and class, duration of HIV infection) were assessed through a pre-tested and standardized questionnaire. The chi-square test was used to test the statistical significance of associations, considering a p-value ≤0.05 as statistically significant. All of the data were analyzed and calculated using the Statistical Package for Social Sciences (SPSS version 20.0) and Microsoft Excel 2016. **Results:** Among the patients, male preponderance was seen with the frequency of 66% (31) and 61.3% (46) with and without GI symptoms respectively. Patients aged 40-49 years old were more frequent with (31.9%) and without (25.3%) GI symptoms. The patients of primary level of education had GI symptoms and had no GI symptoms were 61.7% and 45.3% respectively of the total. Statistically significant (p=0.03) indicating that low CD4+ cell count (≤ 350 cells/mm3) can be considered as an associated risk factor for the occurrence of GI manifestations in HIV infected patients. There was less statistically significant difference in other clinical characteristics between patients with current GI manifestations and without GI manifestations. Here, the statistically significant p-value ≤0.05 is considered. **Conclusion:** This study concluded that, smoking and low CD4 count (<350cell/mm3) were found significantly associated with the occurrence of presenting GI symptoms. Other sociodemographic, lifestyle, and clinical factors were not significantly associated with the occurrence of GI manifestations.

**Keywords**:- Gastrointestinal, manifestations, sociodemographic, HIV, AIDS.

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## INTRODUCTION

Acquired Immune Deficiency Syndrome (AIDS) was first recognized as a new disease in 1981 when increasing numbers of young homosexual men succumbed to unusual opportunistic infections and rare malignancies.[1] AIDS is defined by the development of specified opportunistic infections, cancers, and severe manifestations of HIV itself. CDC category C is the most widely used definition of AIDS.[2] A retrovirus, now termed human immunodeficiency virus type 1 (HIV-1), was subsequently identified as the causative agent of what has since become one of the most devastating infectious diseases to have emerged in recent history.[3] The origin of HIV is a zoonotic infection with simian immunodeficiency viruses (SIV) from African primates. Bush meat hunters were probably the first group to be infected with HIV.[4] The most important factor that increases the risk of sexual transmission of HIV-1 is the number of copies of plasma HIV-1 RNA per mL i.e. viral load, with a 2·4 times increased risk of sexual transmission for every 1 log10 increase.[5] Acute HIV infection, which causes very high plasma viral loads in the first few months, is an important driver of HIV epidemics.[6] A reduction in plasma viral load of 0·7 log10 is estimated to reduce HIV-1 transmission by 50%.[7] Seminal and endocervical viral load independently predict the risk of HIV-1 sexual transmission, after adjustment for plasma viral load.[8] Other factors associated with increased risk of sexual transmission of HIV include sexually transmitted infections (notably genital ulcers of any cause, herpes simplex type-2 infection, and bacterial vaginosis), pregnancy, and receptive anal intercourse.[9] Male circumcision is associated with a reduced risk of sexual transmission of HIV.[10] Findings of some observational studies showed an increased risk of HIV-1 acquisition in women who used long-acting injectable progestogens for contraception, but not with combined oral contraceptives.[11] HIV infects cells bearing CD4 receptors and destroys them. With time there is gradual attrition of the helper-T cell population and, as these cells are pivotal in orchestrating the immune response, the patient becomes susceptible to opportunistic infections. HIV itself is associated with a wide variety of clinical manifestations, and opportunistic diseases add many more. HIV/AIDS has a variety of presentations. In low endemic areas like Bangladesh, it is very difficult to diagnose early because the clinical manifestations mimic many common diseases. HIV-1 was transmitted from apes and HIV-2 from sooty mangabey monkeys.[4] Four groups of HIV-1 exist and represent three separate transmission events from chimpanzees (M, N, and O), and one from gorillas (P). Groups N, O, and P are restricted to West Africa. Group M, which is the cause of the global HIV pandemic, started about 100 years ago and consists of nine subtypes: A–D, F–H, J, and K. Globally, subtype C (which predominates in sub-Saharan Africa and India) accounts for half of the infections and appears to be more readily transmitted. Thus sub-Saharan Africa, especially southern Africa has the highest global burden of HIV (70-80%).[12] Subtype B predominates in Western Europe, the Americas, and Australia. Circulating recombinant subtypes is becoming more common.[12] In Europe, the prevalence of non-B subtypes is increasing because of migration. Subtypes A and D are associated with slower and faster disease progression, respectively.

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Regions have marked differences in HIV prevalence, incidence, and dominant modes of transmission.[2] The marked genetic diversity of HIV-1 is a consequence of the error-prone function of reverse transcriptase, which results in a high mutation rate. HIV-1 is the cause of the global HIV pandemic, while HIV-2, which causes a similar illness to HIV-1 but progresses more slowly and is less transmissible, is restricted mainly to western Africa.[13] Despite the availability of antiretroviral that can prevent mother-to-child HIV transmission, just 82% of pregnant women have access to them, resulting in 160,000 new infections among children – well short of the target of less than 40,000. Regarding HIV prevention, the report says that only around 300,000 people worldwide – including 130,000 in the US – are using pre-exposure prophylaxis, although this is at best a rough estimate.[14] Similarly, although people who inject drugs account for a high proportion of new HIV infections in some regions, many lack access to adequate harm reduction services.

### Objective

### General Objective

- To identify the association of gastrointestinal manifestations with sociodemographic, lifestyle, and clinical factors in HIV/AIDS patients.

### Specific Objectives

- To show the association of gastrointestinal manifestations in HIV/AIDS patients with their age, gender, income per month, and education level.
- To identify the association of gastrointestinal manifestations in HIV/AIDS patients with their smoking status, alcohol consumption, and physical activity level.
- To see the association of gastrointestinal manifestations in HIV/AIDS patients with their clinical status.

## MATERIAL AND METHODS

This observational cross-sectional analytical study was conducted at the ART corner and Department of Gastroenterology, Bangabandhu Sheikh Mujib Medical University, Shahbag, Dhaka among adult HIV-infected or AIDS patients aged more than 18 years. A total of 122 patients were taken as per inclusion criteria. The study duration was from March 2018 to February 2019. Continuous variables were reported as the mean ± standard deviation. Absolute and relative frequencies of GI manifestations were computed. Numerical variables were expressed as mean and standard deviation, whereas categorical variables as a percentage. The chi-square test was used to test the statistical significance of associations, considering a p-value ≤0.05 as statistically significant. The correlation of several GI symptoms with CD4 count was done by the Spearman rank test. Firstly, informed written consent was taken from the respondents. Each patient was evaluated by history taking, physical examination, and reviewing previous medical records and investigations to identify GI manifestations at present and during the initial diagnosis of HIV/AIDS according to Rome III criteria. Sociodemographic variables (gender, age, income, and education level), lifestyle variables (smoking status, risk consumption of alcohol, and physical activity level), and clinical variables (antiretroviral therapy – duration and class, duration of HIV infection) were assessed through a pre-tested

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and standardized questionnaire. The patient's height and weight were measured and BMI was calculated. Necessary investigations (if required as per management protocol) including endoscopy, colonoscopy, and CD4 cell count were done or previous investigations including CD4 cell count report were collected. All of the data were analyzed and calculated using the Statistical Package for Social Sciences (SPSS version 20.0) and Microsoft Excel 2016.

**Inclusion Criteria**

- Adults with HIV infection or AIDS aged 18 years or above, regardless of their duration of illness or ART status
- Patients who had given consent to participate in the study.

**Exclusion Criteria**

- Pregnant women and lactating mother
- Patients who did not give consent to participate in the study.
- Patients with other chronic diseases etc.

## RESULTS

This table shows the association of sociodemographic factors of HIV-infected patients with the occurrence of GI manifestations. Among the patients, male preponderance was seen with the frequency of 66% (31) and 61.3% (46) with and without GI symptoms respectively. Patients aged 40-49 years old were more frequent with (31.9%) and without (25.3%) GI symptoms. 29 (61.7%) patients with GI symptoms and 42 (56.0%) patients without GI symptoms were surveyed. The patients of primary level of education had GI symptoms and had no GI symptoms were 61.7% and 45.3% of the total. [Table 1]

This table shows the association of lifestyle characteristics of HIV-infected patients with the occurrence of GI manifestations. Among the patients who had GI manifestations, 24 (51.1%) were smokers and 23 (48.9%) were nonsmokers, and among the patients who had no GI manifestations, 22 (29.3%) were a smoker and 53 (70.7%) were nonsmoker and the difference was statistically significant (p=0.016) indicating that smoking can be considered as an associated risk factor for the occurrence of GI manifestations in HIV infected patients. There was no statistically significant difference in other lifestyle characteristics between patients with GI manifestations and without GI manifestations including – smoking status, alcohol consumption, and physical activity level. [Table 2]

This table shows the association of clinical characteristics of HIV-infected patients with the occurrence of GI manifestations. Among the patients who had GI manifestations, 10 (34.5%) had CD4+ cell count ≤ 350 and 19 (65.5%) had CD4+ cell count > 350 and among the patients who had no GI manifestations, 4 (11.8%) had CD4+ cell count ≤ 350 and 30 (88.2%) had CD4+ cell count > 350 and the difference was statistically significant (p=0.03) indicating that low CD4+ cell count (≤ 350 cells/mm3) can be considered as an associated risk factor for the occurrence of GI manifestations in HIV infected patients. There was no statistically significant difference in other clinical characteristics between patients with current GI manifestations and without GI manifestations including – ART use, type and duration of ART, duration of HIV infection, and patient's nutritional status (BMI). [Table 3]

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**Table 1:** Association of gastrointestinal manifestations with sociodemographic factors of HIV-infected patients (N=122).

| Sociodemographic Factors | | With GI symptoms N (%) | Without GI symptoms N (%) | p-value |
|---|---|---|---|---|
| Gender | Male | 31 (66.0) | 46 (61.3) | 0.357 |
| | Female | 15 (31.9) | 29 (38.7) | |
| | Other | 1 (2.1) | 0 (0.0) | |
| Age (Years) | 19-29 | 6 (12.8) | 13 (17.3) | 0.360 |
| | 30-39 | 14 (29.8) | 31 (41.3) | |
| | 40-49 | 15 (31.9) | 19 (25.3) | |
| | 50 or more | 12 (25.5) | 12 (16.0) | |
| Income (Tk/month) | <15000 | 29 (61.7) | 42 (56.0) | 0.131 |
| | 15000-50000 | 16 (34.0) | 33 (44.0) | |
| | >50000 | 2 (4.3) | 0 (0.0) | |
| Level of education | Primary | 29 (61.7) | 34 (45.3) | 0.087 |
| | Secondary | 15 (31.9) | 28 (37.3) | |
| | Higher Secondary | 1 (2.1) | 11 (14.7) | |
| | Graduate or above | 2 (4.3) | 2 (2.7) | |

**Table 2:** Association of gastrointestinal manifestations with lifestyle characteristics of HIV-infected patients (N= 122).

| Lifestyle factors | | With GI symptoms N (%) | Without GI symptoms N (%) | p-value |
|---|---|---|---|---|
| Smoking status | Nonsmoker | 23 (48.9) | 53 (70.7) | 0.016* |
| | Smoker | 24 (51.1) | 22 (29.3) | |
| Risk consumption of alcohol | Yes | 0 (0.0) | 2 (2.7) | 0.259 |
| | No | 47 (100.0) | 73 (97.3) | |
| Physical activity level | Active | 19 (40.4) | 28 (37.3) | 0.773 |
| | Sedentary | 28 (59.6) | 47 (62.7) | |

A chi-square test was done to measure the level of significance; * indicates a significant result.

**Table 3:** Association of gastrointestinal manifestations with clinical characteristics of HIV-infected patients (N= 122).

| Clinical Characteristics | With GI symptoms N (%) | Without GI symptoms N (%) | p-value |
|---|---|---|---|
| Antiretroviral therapy | | | |
| Yes | 47 (85.5) | 75 (93.8) | |
| NNRTI | | | |
| Yes | 42 (89.4) | 69 (92.0) | 0.621 |
| No | 5 (10.6) | 6 (8.0) | |
| PI | | | |
| Yes | 5 (10.6) | 6 (8.0) | 0.621 |
| No | 42 (89.4) | 69 (92.0) | |

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| | | | |
|---|---|---|---|
| Time of HIV infection (years) | | | |
| < 1 | 12 (25.5) | 16 (21.3) | 0.866 |
| 1 – 3 | 10 (21.3) | 17 (22.7) | |
| > 3 | 25 (53.2) | 42 (56.0) | |
| Time of ART use | | | |
| < 1 | 12 (25.5) | 17 (22.7) | 0.889 |
| 1 – 3 | 12 (25.5) | 18 (24.0) | |
| > 3 | 23 (48.9) | 40 (53.3) | |
| CD4+ lymphocyte count | | | |
| ≤ 350 cells/mm3 | 10 (34.5) | 4 (11.8) | 0.030* |
| > 350 cells/mm3 | 19 (65.5) | 30 (88.2) | |
| Nutritional status (BMI) | | | |
| Underweight | 9 (19.1) | 12 (16.0) | 0.411 |
| Normal weight | 25 (53.2) | 47 (62.7) | |
| Overweight | 10 (21.3) | 15 (20.0) | |
| Obese | 3 (6.4) | 1 (1.3) | |

A chi-square test was done to measure the level of significance; * indicates a significant result.

**Table 4:** Correlation of CD4 values with the number of GI manifestations by Spearman rank test (n=63)

| **Variables** | **n** | **r** | **p-value** |
|---|---|---|---|
| CD4 | | | |
| GI problems | 63 | -0.177 | 0.166 |

GI: Gastrointestinal; r: correlation coefficient

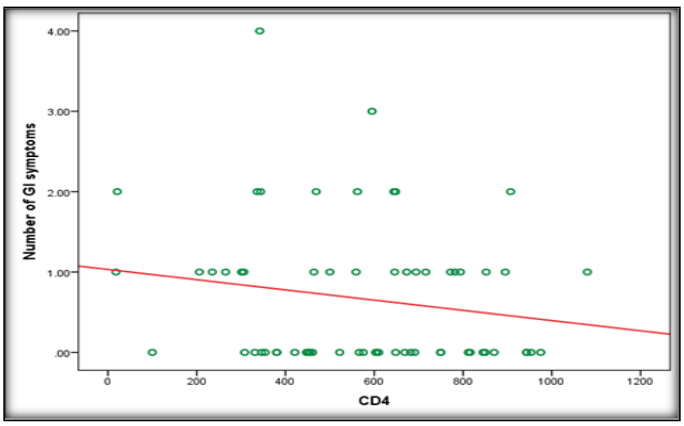


**Figure 1:** Correlation of CD4 cell count with the number of GI manifestations.

Data on CD4 was found in 63 patients of HIV to analyze the correlation between CD4 number and the number of GI manifestations among them. The scattered diagram in Figure 9 and the Spearman rank correlation test showed no significant correlation between CD4 number and the number of GI manifestations. The negative correlation indicates that an increased CD4 level would be followed by less number of GI manifestations (r = -0.177). [Table 4] & [Figure 1]

## DISCUSSION

The present cross-sectional analytical study was conducted in the Department of Gastroenterology and ART corner of OPD, BSMMU aimed to identify the prevalence of gastrointestinal manifestations in HIV/AIDS patients and to identify their association with

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sociodemographic (age, sex, income, and education level), lifestyle (smoking status, alcohol consumption, and physical activity level) and clinical factors (antiretroviral therapy, time of HIV infection, CD4 lymphocyte count and nutritional status). The GI tract is a major site of disease in HIV infection. Diarrhea, the most common GI complaint, can occur during both acute HIV infection and advanced disease. Within days of HIV infection, an intense infiltration of virus-laden lymphocytes occurs in the bowel wall and may manifest as diarrhea during seroconverting illness.[15] This study showed the association of sociodemographic factors of HIV-infected patients with the occurrence of GI manifestations. Among the patients, male preponderance was seen with the frequency of 66% (31) and 61.3% (46) with and without GI symptoms respectively. Patients aged 40-49 years old were more frequent with (31.9%) and without (25.3%) GI symptoms. 29 (61.7%) patients with GI symptoms and 42 (56.0%) patients without GI symptoms were surveyed. The patients of primary level of education had GI symptoms and had no GI symptoms were 61.7% and 45.3% of the total. In another study, regarding sociodemographic characteristics, the presence of three or more GIS was associated with the male sex (50%) and female (32%) was found which is similar to our study.[16] Our study also showed the association of lifestyle characteristics of HIV-infected patients with the occurrence of GI manifestations. Among the patients who had GI manifestations, 24 (51.1%) were smokers and 23 (48.9%) were nonsmokers, and among the patients who had no GI manifestations, 22 (29.3%) were a smoker and 53 (70.7%) were nonsmoker and the difference was statistically significant (p=0.016) indicating that smoking can be considered as an associated risk factor for the occurrence of GI manifestations in HIV infected patients. There was no statistically significant difference in other lifestyle characteristics between patients with GI manifestations and without GI manifestations including – smoking status, alcohol consumption, and physical activity level. In our study smoking and low CD4 count (<350cell/mm3) were found significantly associated with the occurrence of present GI symptoms. Other sociodemographic, lifestyle, and clinical characteristics including age, gender, education level, income, alcohol consumption, physical activity, ART use, type and duration of ART, duration of HIV infection, and patient's nutritional status were not significantly associated with the occurrence of GI manifestations.[16] In a different study, female gender (IR 2.29, 95% CI 1.63 to 3.22) and smoking status (IR 1.93, 95% CI 1.30 to 2.88) were risk factors for the presence of three or more GI symptoms in HIV/AIDS patients. In our study, no significant correlation was found between CD4 number and the number of GI problems but there was a significant reduction in the occurrence of GI manifestations while on ART.[17] In another study, it was found that only 68 data of CD4 among 647 patients of HIV/AIDS showed a significant correlation between CD4 level and gastrointestinal problems (p = 0.04). With the advent of highly active antiretroviral therapy (HAART), opportunistic etiologies, along with HIV enteropathy, have dramatically decreased. Although HAART has dramatically changed the course of HIV, it has yet to fully restore normal life expectancy among those infected.[18] Part of the reason may be residual involvement of the GI tract; ongoing immune activation and

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inflammation may play a role in the development of conditions contributing to excess GI morbidity in this population.[15] Further studies on HIV-induced GI problems and their associated risk factors are needed. Opportunistic infections occur as the CD4 T cell count falls below 100–200 cells/mm3 including a myriad of viral, bacterial, fungal, and parasitic pathogens.[19] Beyond the risk for opportunistic pathogens, HIV itself alters the structure and function of the GI tract.[20] Noted histological changes in the GI tracts of HIV patients in the absence of other defined infectious or malignant etiologies and termed the condition "HIV enteropathy". Different studies have reported GI symptoms in 50–70% of HIV-infected persons, with even higher percentages among those residing in the developing world.[19] In our study, no significant correlation was found between CD4 number and the number of GI problems but there was a significant reduction in the occurrence of GI manifestations while on ART.[17] Another study showed that only 68 data of CD4 among 647 patients of HIV/AIDS showed a significant correlation between CD4 level and gastrointestinal problems (p = 0.04). With the advent of highly active antiretroviral therapy (HAART), opportunistic etiologies, along with HIV enteropathy, have dramatically decreased. Although HAART has dramatically changed the course of HIV, it has yet to fully restore normal life expectancy among those infected.[18] Part of the reason may be residual involvement of the GI tract; ongoing immune activation and inflammation may play a role in the development of conditions contributing to excess GI morbidity in this population [15]. Further studies on HIV-induced GI problems and their associated risk factors are needed.

**Limitations of the Study**

The sample size of the study was smaller and also the study period was relatively shorter. The participants were from one center, so the result cannot be generalized to the reference population.

## CONCLUSIONS

This study concluded that, smoking and low CD4 count (<350cell/mm3) were found significantly associated with the occurrence of present GI symptoms. Other sociodemographic, lifestyle, and clinical characteristics including age, gender, education level, income, alcohol consumption, physical activity, and patient's nutritional status were not significantly associated with the occurrence of GI manifestations.

**Recommendation**

Further studies should be conducted involving a large sample size and multiple centers. For further study, the addition of other noninvasive and invasive methods/tests may be useful to reach the final gastrointestinal diagnosis and to assess the severity and degree of involvement of the GI tract by HIV. Clinicians including gastroenterologists and health care professionals should be aware of the early diagnosis, and treatment to prevent its further dissemination.

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