Tropical Doctor
2017, Vol. 47(1) 44–48

DOI: 10.1177/0049475515626338
tdo.sagepub.com
SAGE

Role of intestinal dysfunction in the nutritional compromise seen in human immunodeficiency virus-infected adults in rural India

Rita Isaac[1], Biswajit Paul[1], FS Geethanajali[2], Gagandeep Kang[3] and Christine Wanke[4]

Abstract

Human immunodeficiency virus (HIV) disease progression is often marked by significant weight loss with or without chronic diarrhoea. We studied the extent of intestinal dysfunction using a D-xylose absorption test and association with nutritional compromise as measured by body mass index (BMI) and serum antioxidants levels in HIV-infected individuals through a cross-sectional survey of 45 ART naïve, HIV-positive and 45, age–socioeconomic status matched negative controls in a rural population in India. More than 40% of HIV-positive and HIV-negative participants had intestinal dysfunction (42.2% vs. 44.4%). However an increasing gradient of low D-xylose absorption was noted with decreasing CD4 counts (32%, 50% and 58.3% among those with >350, 200–350 and <200 cells/mm^3, respectively). Multivariate analysis revealed a significant association between intestinal dysfunction and low BMI ($P = 0.03$) independent of HIV infection and calorie intake per day ($P = 0.02$). Weight loss in HIV-infected individuals should be investigated for intestinal dysfunction especially in low resource settings.

Keywords

Disease prevention, epidemiology, Asia, diagnosis

Introduction

In recent years human immunodeficiency virus (HIV) infection has become a manageable, chronic disease. Recent research on HIV has focused on co-morbidities and other changes that may jeopardize the quality of life of infected patients. It has been shown that HIV infection alters the structure of the gastrointestinal tract and, in particular, the function of the gut mucosa as a protective barrier.[1–3] HIV enteropathy denotes disruption of intestinal endothelial integrity in HIV-infected individuals, pathologically characterised by inflammation in the epithelium and lamina propria of the intestine and villous atrophy; many factors, including both host-related and environmental, can aggravate and lead to its development. Previous studies, mostly done in rich countries, have shown that HIV enteropathy, though mechanisms leading to it are not well understood, contributes to malabsorption of macro- and micro-nutrient deficiencies and to progressive weight loss.[4–8] Furthermore it is possible that altered intestinal function may lead to poor absorption of antiretroviral and anti-tuberculosis drugs, resulting in treatment failure.[9,10] Significant advances have been made concerning intestinal pathology associated with HIV infection,[11] but, to our knowledge, little is known about the magnitude of intestinal dysfunction in the HIV-infected population. The consequence of this and other contributing factors in resource-poor countries including India have not been much described. This study was undertaken to measure the association of intestinal dysfunction in HIV-infected individuals with nutritional

[1]Associate Professor, RUHSA Department, Christian Medical College, Vellore, Tamil Nadu, India
[2]Professor, Department of Clinical Biochemistry, Christian Medical College, Vellore, Tamil Nadu, India
[3]Professor, Department of Gastrointestinal Sciences, Christian Medical College, Vellore, Tamil Nadu, India
[4]Professor, Department of Public Health and Community Medicine, Tufts University School of Medicine, Boston, Massachusetts, USA

Corresponding author:
Rita Caroline Isaac, Professor and Head, RUHSA Department, Christian Medical College, RUHSA Campus, Vellore 632209, Tamil Nadu, India.
Email: rita.isaac@cmcvellore.ac.in

status and low serum/plasma levels of antioxidant micronutrients including retinol, β-carotenoids, vitamin E and mineral zinc, comparing levels with healthy sero-negative controls in a rural population in India.

Methods

Study setting

Our study was carried out in 2006 by the Rural Unit of Health and Social Affairs (RUHSA), an outreach community health centre of the Christian Medical College, Vellore, Tamil Nadu, India. The target population is mainly agrarian with many being subsistent farmers and labourers. The scarcity of water and lack of access to modern farming technology have made many change their occupations and a significant proportion of young men have migrated to neighbouring towns and cities seeking jobs. Only approximately 60% of men and 40% of women in the study population were literate. The study was approved by the institutional review boards at the Christian Medical College, India and at Tufts University School of Medicine, Boston, USA.

Subjects

A cross-sectional survey was conducted among 45 consenting HIV-infected participants who attended the RUHSA HIV clinic and 45 age and socioeconomic status matched HIV-negative, neighbourhood, population controls. The eligibility criteria for the HIV-positive participants were: HIV infection confirmed by two National Aids Control Organisation (NACO) recommended rapid tests; ART naïve; and no history of end-stage renal disease, chronic liver disease or severe AIDS-related illness.

Variables

The HIV disease status was assessed by CD4 cell count using flow cytometry. BMI (kg/m^2) was calculated from weight and height measured on a single scale. The 5 g oral D-xylose absorption urine test was used as a marker of intestinal dysfunction. Subjects were instructed to empty their bladder completely at 6 am and then drink 5 g of D-xylose in water. They were allowed to eat breakfast 30 min afterwards, and instructed to drink a minimum of 1 L of water during the next 4 h and to collect all their urine passed in a graduated bottle for 5 h from the time of ingestion of D-xylose. The total urine output was measured and an aliquot of urine sample was examined to estimate D-xylose levels. The test was considered unreliable if the urine output over the first 5 h was <500 mL. D-xylose absorption is considered normal when 20% or more of the oral dose is excreted in 5 h in the urine. High performance liquid chromatography (HPLC) was used to measure serum levels of retinol, β-carotenoids and vitamin E, and flame atomic absorption spectroscopy was used to measure serum zinc levels.

Dietary intake was assessed using 24 h recall and a Food Frequency Questionnaire developed by the National Institute of Nutrition (NIN), India. The study nutritionist, with the help of standard food measures and food models, made an assessment of portion sizes and dietary intake. This was analysed manually using the caloric value and micronutrient content in the raw ingredients of recipe based food items in India, published by NIN.[12] As the adequacy of intake of micronutrients of interest in this study is dependent on food diversity in the long-term dietary intake, we calculated daily average intake of micronutrients from the Food Frequency Questionnaire (a measure of long-term usual dietary intake) and 24 h recall (a feasible and convenient measure).

Statistical analysis

Descriptive analysis of socio-demographic characteristics of the participants was done using frequencies, marginal percentages, means, standard deviations, medians and percentiles. BMI, dietary intake, serum retinol, β-carotenoids, vitamin E and zinc levels, D-Xylose urine levels in HIV-positive cases and HIV-negative controls were compared using the χ^2 statistics for categorical variables, the t-test for normally distributed continuous variables and the Mann–Whitney U test for non-normally distributed continuous variables. The median (interquartile range) values of dietary intake and micronutrient levels are reported since the data were not normally distributed. Any association of abnormal D-Xylose absorption with sex, BMI, serum micronutrients and CD4 levels was checked using parametric and non-parametric tests. Multivariate linear regression was performed using a generalised linear model to estimate the association between D-xylose absorption as an indicator of intestinal function and BMI, adjusting for average calorie intake per day and HIV disease. The data were analysed using SPSS version 17 (Chicago, IL, USA).

Results

The study subjects consisted of 45 HIV-positive patients and 45 matched HIV-negative neighbourhood controls. The mean age of the participants was 30.2 ± 8.3 years with 25% aged less than 25 years. Of the HIV-infected participants, $>50\%$ (26 [57.8%])

Table 1. Comparing BMI, dietary intake, serum retinol, β-carotenoids, vitamin E and zinc levels, low D-Xylose level in the urine in HIV-positive cases and HIV-negative controls.

Variables	HIV-positive (n = 45)	HIV-negative (n = 45)	*P* value
BMI, mean (SD)	20.3 (3.3)	22.02 (4.3)	0.04*
Average dietary intake per day, median (25, 75 percentile)			
Total calories	1499 (1197, 1937)	1770 (1331, 2442)	0.06
Retinol (μg/d)	239.9 (165.4, 340.5)	231.1 (173.9, 343.2)	0.97
Beta carotenoids (μg/d)	411(323.4, 648.8)	482.7(316.8, 651.9)	0.79
Vitamin E (mg/d)	4.2 (3.5, 5.9)	4.9 (3.5, 6.3)	0.99
Zinc (mg/d)	4.8 (3.5, 6.4)	5.83 (4.5, 9.1)	0.02*
Serum micronutrient levels, median (25, 75 percentile)			
Retinol (nmol/mL)	0.255 (0.18, 0.41)	0.316 (0.22, 0.44)	0.27
Beta carotenoids (μg/d)	0.694 (0.44, 1.09)	0.809 (0.57, 1.11)	0.09
Vitamin E (mg/L)	4.18 (1.07, 5.96)	4.14 (3.18, 5.7)	0.23
Zinc (μg/d)	108 (89.5, 124.5)	117 (100, 148.2)	0.02*
D-Xylose in urine, <20% of ingested, n (%)	19 (42.2)	20 (44.4)	0.5

were women and approximately 50% were of low socioeconomic strata as indicated by their poor employment status, housing facility and educational status.

The mean BMI of HIV-positive participants was $20.3 \pm 3.3\,kg/m^2$ and that of HIV-negative participants 22.02 ($4.3\,kg/m^2$), a difference which was statistically significant ($P = 0.04$) and the median CD4 cell count of seropositive participants was 381. A total of 42.2% of HIV-positive and 44.4% HIV-negative participants had intestinal dysfunction as indicated by low D-xylose absorption and this difference was not statistically significant (Table 1).

The average daily intake of total calories was found to be lower among HIV-positive participants ($P = 0.06$). The median daily dietary intake of retinol (RDA: 500 μg/day), vitamin E (RDA: 20 mg/day) and zinc (RDA: 10 mg/day) were lower than the recommended dietary allowance in both HIV-positive and HIV-negative participants, and the zinc intake was significantly lower in HIV-positive participants ($P = 0.02$) Table 1).

The prevalence of D-xylose malabsorption was similar in both men and women (54.5% vs. 58.7%). Low D-xylose absorption was significantly associated with BMI ($P = 0.03$) (Table 2). The median serum levels of retinol (<0.349 nmol/mL) and vitamin E (<5 mg/dL) were low in both groups and β-carotenoids (>0.5 micromol/L) was adequate in both groups, there being no statistically significant difference. The median serum Zinc levels was adequate in both groups (>70 μg/dL), however the levels were significantly lower in HIV infected participants ($p = 0.02$). The data did not show a statistically significant association between low D-xylose absorption and low serum levels of micronutrients. A significant association however was found between CD4 count and low D-xylose absorption ($P = 0.029$), and D-xylose absorption was found to be worse with decreasing CD4 count in HIV-positive participants as follows: 32%, 50% and 58.3% among those with CD4 count of >350, 200–350 and <200 cells/mm^2, respectively (Table 2). The participants, both HIV-infected and not infected, who showed low D-xylose absorption had, on average, a BMI 1.886 lower compared to those with normal absorption, adjusting for HIV disease status and average calorie intake per day. This association was statistically significant ($P < 0.02$) (Table 3).

Discussion

A similar number of participants, whether HIV-positive or negative, showed evidence of intestinal dysfunction. This was, however, worse with advanced HIV disease (defined by decreasing CD4 count). This suggests an underlying prevalence of enteropathy among the rural population in India, and was first recognised in the 1950s and 1960s with the advent of small bowel biopsy, and the changes noted were traditionally termed tropical enteropathy.[13–15] Our study further found that the average total calorie intake of HIV-positive participants was lower than HIV-negative comparisons although the measured difference only showed near statistical significance ($P = 0.06$) (Table 1).

Prevalent co-existing tropical enteropathy, HIV-induced intestinal dysfunction, poor socioeconomic status and poor access to good nutrition (as indicated by less than adequate daily intake of calories) make the HIV-positive population in India more vulnerable

Table 2. Association of abnormal D-Xylose absorption with sex, BMI, serum micronutrients, CD4 (HIV-positive participants only) ($n = 90$).

Variables	Low urine D-xylose (<20%), n/Mean	%/SD	Normal urine D-Xylose	%/SD	*P* value
Sex					
Male	20.0	54.5	24.0	45.5	0.8
Female	19.0	58.7	27.0	41.3	
BMI	20.07	0.55	21.9	0.6	0.03*
Serum retinol	0.31	0.03	0.32	0.02	0.8
Serum β carotenoids	0.79	0.08	0.87	0.06	0.4
Serum vitamin E	4.60	0.55	4.40	0.28	0.66
Serum zinc	111.95	4.9	114.58	4.29	0.68
CD4	282.0	43.0	451.0	56	0.029*
CD4 categorised					
<200 cells/mm^3	7.0	58.3	5.0	41.7	
200–350 cells/mm^3	4.0	50.0	4.0	50.0	
>350 cells/mm^3	8.0	32.0	17.0	68.0	

Table 3. Multivariate analysis assessing the association between low D-xylose absorption, calorie intake and HIV disease and BMI.

Predictor variables	B coefficient*	SE	*P* value
Intercept	21.964	1.509	0.000
D-Xylose absorption			
Low	−1.886	0.818	0.024*
Normal	–		
Average daily calorie intake	0.000	0.001	0.499
HIV-positive cases	−1.760	0.842	0.040*

*Linear regression coefficient measures the change in BMI (dependent variable) per unit change in predictor variables.

to nutritional compromise and rapid progression of disease. This may also be true in most low-income countries. Low to marginal serum/plasma levels of antioxidant micronutrients are known to lead to rapid disease progression and increasing morbidity and mortality in an HIV-infected population in a poor resource setting.[16]

Our exploratory cross-sectional survey was an attempt to pilot test the hypothesis that increased intestinal dysfunction could be a risk factor for nutritional compromise, as signified by a high prevalence of low serum/plasma levels of micronutrients and low BMI in HIV-positive individuals. The magnitude of intestinal dysfunction and its association with the stage of disease and other risk factors among HIV-infected individuals needs to be known for their effective management. We expected a higher prevalence of intestinal dysfunction in HIV-positive participants although this clearly worsens as the disease progresses, which is no surprise.[17,18]

Limitations of our study include the small sample size and the use of D-xylose as a marker of intestinal function, as this may not be as good as, for example, 72 h faecal fat and the lactuolose/mannitol intestinal permeability test. Nonetheless, our study had well-matched controls and precisely measured dietary intake data which have not been available in previous studies.

In summary our study revealed a disastrous association with poverty, poor dietary intake, increased intestinal malabsorption, low serum levels of antioxidants and low BMI in the HIV-infected population in rural India. This warrants immediate attention and appropriate management.

Acknowledgements

We acknowledge with thanks the grant support and expert advice received from Dr. Sherwood L Gorbach, Professor and Former Director of Nutrition and Infection Division, Department of Public Health and Community Medicine, Tufts University School of Medicine, Boston. We appreciate the contributions made by the research coordinators and outreach health workers. Special thanks go to all the participants for their cooperation and willingness to participate in the study.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This research was supported by the National Institute of Health, Fogarty International Centre Programme 43tw00237.

References

1. Lima AA, Silva TM, Gifoni AM, et al. Mucosal injury and disruption of intestinal barrier function in HIV-infected individuals with and without diarrhea and cryptosporidiosis in northeast Brazil. *Am J Gastroenterol* 1997; 92: 1861–1866.
2. Pernet P, Vittecoq D, Kodjo A, et al. Intestinal absorption and permeability in human immunodeficiency virus-infected patients. *Scand J Gastroenterol* 1999; 34: 29–34.
3. Clayton F, Kotler DP, Kuwada SK, et al. Gp120-induced Bob/GPR15 activation: a possible cause of human immunodeficiency virus enteropathy. *Am J Pathol* 2001; 159: 1933–1939.
4. Grinspoon S and Mulligan K. Weight loss and wasting in patients infected with human immunodeficiency virus. *Clin Infect Dis* 2003; 36(Suppl. 2): 69–78.
5. Wheeler DA, Gibert CL, Launer CA, et al. Weight loss as a predictor of survival and disease progression in HIV infection. Terry Beirn Community Programs for Clinical Research on AIDS. *J Acquir Immune Defic Syndr Hum Retrovirol* 1998; 18: 80–85.
6. Kotler DP. Human immunodeficiency virus-related wasting: malabsorption syndromes. *Semin Oncol* 1998; 25: 70–75.
7. Crum-Cianflone NF. HIV and the gastrointestinal tract. *Infect Dis Clin Pract (Baltim Md)* 2010; 18: 283–285.
8. Luangjaru S, Ruxrungtham K, Wisedopas N and Mahachai V. D-xylose absorption in non-chronic diarrhea AIDS patients with the wasting syndrome. *J Med Assoc Thai* 2003; 86(Suppl. 2): S477–483.
9. Brantley RK, Williams KR, Silva TM, et al. AIDS-associated diarrhea and wasting in Northeast Brazil is associated with subtherapeutic plasma levels of antiretroviral medications and with both bovine and human subtypes of Cryptosporidium parvum. *Braz J Infect Dis* 2003; 7: 16–22.
10. Gurumurthy P, Ramachandran G, Kumar AKH, et al. Malabsorption of Rifampin and Isoniazid in HIV-infected patients with and without Tuberculosis. *Clin Inf Dis* 2004; 38: 280–283.
11. Maresca P, Mahfoud R, Garmy N, Kotler DP, Fantini J and Clayton F. The virotoxin model of HIV-1 enteropathy: inhibition of gp 120-induced experimental enteropathy by a synthetic soluble analog of galactosylceramide (GalCer), anti-Galcer and anti-GPR15 Bob antibodies. *J Biomed Sci* 2003; 10: 156–166.
12. Gopalan C, *et al*. Nutritive value of Indian foods. Published by National Institute of Nutrition and Indian Council of Medical Research, 1999.
13. Campbell DI, Lunn PG and Elia M. Age-related association of small intestinal mucosal enteropathy with nutritional status in rural Gambian children. *Br J Nutr* 2002; 88: 499–505.
14. Haghighi P and Wolf PL. Tropical sprue and subclinical enteropathy: a vision for the nineties. *Crit Rev Clin Lab Sci* 1997; 34: 313–341.
15. Wood GM, Gearty JC and Cooper BT. Small bowel morphology in British Indian and Afro-Caribbean subjects: evidence of tropical enteropathy. *Gut* 1991; 32: 256–259.
16. Baum MK, Shor-Posner G, Lu Y, et al. Micronutrients and HIV-1 disease progression. *AIDS* 1995; 9: 1051–1056.
17. Ribeiro Machado F, Gonzaga Vaz Coelho L, Chausson Y and Greco DB. Fat malabsorption assessed by 14C-triolein breath test in HIV-positive patients in different stages of infection: is it an early event? *J Clin Gastroenterol* 2000; 30: 403–408.
18. Murphy B, Taylor C, Crane R, Okong P and Bjarnason I. Comparison of intestinal function in human immunodeficiency virus-seropositive patients in Kampala and London. *Scand J Gastroenterol* 1999; 34: 491–495.

Gastrointestinal bleeding in the tropics: Look for the hookworm

Tropical Doctor
2017, Vol. 47(1) 48–51

DOI: 10.1177/0049475516640192
tdo.sagepub.com
SAGE

Vishal Sharma[1], Deepak Gunjan[1], Puneet Chhabra[2], Ravi Sharma[3], Surinder Singh Rana[4] and Deepak Kumar Bhasin[4]

[1]Assistant Professor, Department of Gastroenterology, Postgraduate Institute of Medical Education and Research, Chandigarh, India
[2]Attending Gastroenterologist, Fortis Hospital, Mohali, Punjab, India
[3]Senior Research Fellow, Postgraduate Institute of Medical Education and Research, Chandigarh, India
[4]Associate Professor, Postgraduate Institute of Medical Education and Research, Chandigarh, India

Corresponding author:
Vishal Sharma, Department of Gastroenterology, PGIMER, Chandigarh, India.
Email: docvishalsharma@gmail.com