CIRCULATING (1→3)-β-D-GLUCAN AS A MARKER OF M`ICROBIAL TRANSLOCATION IN HIV INFECTION

Vikram Mehraj[1,2], Rayoun Ramendra[1,2,3], Cecilia Costiniuk[1,2], Bertrand Lebouché[1,2,4], Rosalie Ponte[1,2], Réjean Thomas[5], Jason Szabo[1,5], Pierre Coté[6], Roger LeBlanc[7], Jean-Guy Baril[6], Cécile Tremblay[8,9], Nicole F Bernard[1,2], Donald C Sheppard[2,3], and Jean-Pierre Routy[1, 2,10] for the Montreal Primary HIV-infection Study Group

1. Chronic Viral Illness Service, McGill University Health Centre, Montreal, QC, Canada; 2. Research Institute, McGill University Health Centre, Montreal, QC, Canada; 3. Department of Microbiology and Immunology, McGill University, Montreal, QC, Canada; 4. Department of Family Medicine, McGill University, Montreal, QC, Canada; 5. Clinique Médicale l'Actuel, Montréal, QC, Canada; 6. Clinique Médicale Quartier Latin, Montréal, QC, Canada; 7. Clinique Médicale OPUS, Montréal, QC, Canada; 8. Centre de recherche du Centre Hospitalier de l'Université de Montréal, Montréal, QC, Canada; 9. Département de microbiologie, infectiologie et immunologie, Université de Montréal, Montréal, QC, Canada; 10. Division of Hematology, McGill University Health Centre, Montreal, QC, Canada

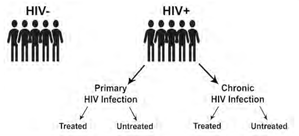
254

Introduction

HIV infection is linked to gut damage and translocation of microbial products into the systemic circulation contributing to immune activation. Bacterial products and host acute phase proteins such as LPS, LBP and sCD14 have been used as markers of microbial translocation in HIV infection; however such utility of fungal antigens has not been defined. We therefore sought to determine the relationship of the fungal antigens (1→3)-β-D-glucan (βDG) and galactomannan with markers of microbial translocation, inflammation and disease progression in early/primary (PHI) and chronic (CHI) HIV infection.

Methods

A total of 131 participants without suspicion of fungal infection and/or gastrointestinal symptoms were assessed in a cross-sectional analysis, including 74 PHI, 36 CHI and 21 uninfected controls. A subgroup of PHI and CHI participants on ART was also assessed. Plasma βDG and galactomannan levels were quantified using Fungitell® and Platelia™ assays, respectively. Plasma βDG levels were compared with age, sex, viral load, CD4 and CD8 T-cell counts, CD4/CD8, markers of gut damage (I-FABP), microbial translocation (LPS, LBP and sCD14), inflammation (IL1-β, IL-6, IL-8 and TNF-α) and Kynurenine/Tryptophan ratio. Univariate and multivariate analyses were conducted at 5% α.



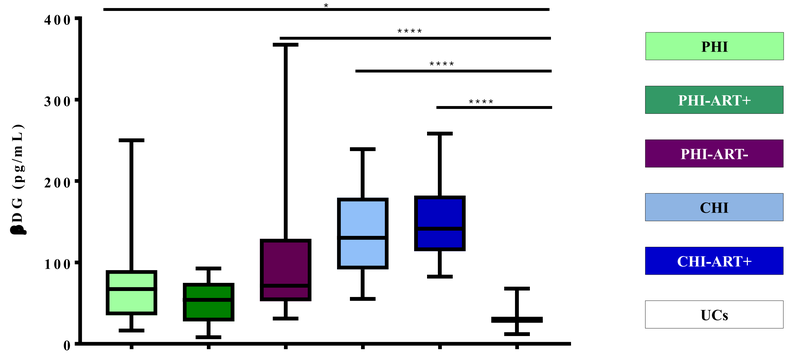
Results

Descriptive Characteristics of Study Participants (n=131)

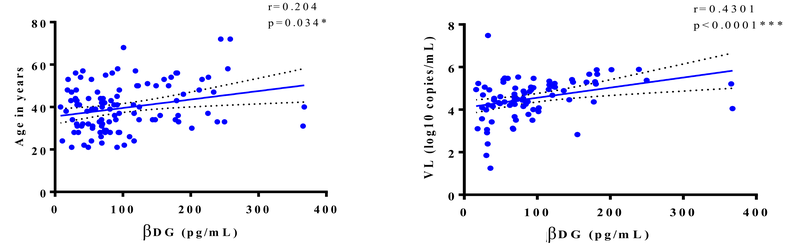
Characteristics	PHI (n= 39)	PHI-ART+ (n = 13)	PHI-ART- (n = 22)	CHI (n = 22)	CHI-ART+ (n = 14)	UCs (n = 21)
Age in years						
Median (IQR)	34 (28-44)	39 (29-44)	35 (31-43)	38 (33-50)	54 (47-60)	46 (35-52)
Range	21-57	22-58	21-56	22-56	26-72	23-69
Sex						
Men, n (%)	38 (97.4)	13 (100)	21 (95.5)	17 (77.3)	13 (92.9)	15 (71.4)
Women, n (%)	1 (2.6)	0 (0)	1 (4.5)	5 (22.7)	1 (7.1)	6 (28.6)
CD4 cells/µL						
Median (IQR)	480 (370-640)	530 (430-720)	490 (297-874)	220 (35-345)	520 (382-621)	821 (519-1020)
Range	220-1680	366-912	210-1110	3-489	161-1083	281-1045
CD8 cells/µL						
Median (IQR)	810 (620-1020)	590 (431-950)	745 (615-977)	770 (406-1147)	710 (544-890)	370 (273-535)
Range	279-2590	268-1325	280-1460	54-1425	300-1213	188-843
CD4/CD8						
Median (IQR)	0.6 (0.4-0.9)	0.7 (0.6-1.3)	0.6 (0.4-1.1)	0.2 (0.1-0.4)	0.7 (0.5-0.9)	2.1 (1.2-3.0)
Range	0.2-2.8	0.5-1.9	0.2-3.3	0.1-1.0	0.4-1.2	0.4-4.0
VL, log10 copies/mL						
Median (IQR)	4.4 (3.7-5.0)	<1.7	4.5 (4.2-5.1)	5.1 (4.4-5.5)	<1.7	NA
Range	1.3-7.5	NA	2.8-5.5	3.9-5.5	NA	NA

Results

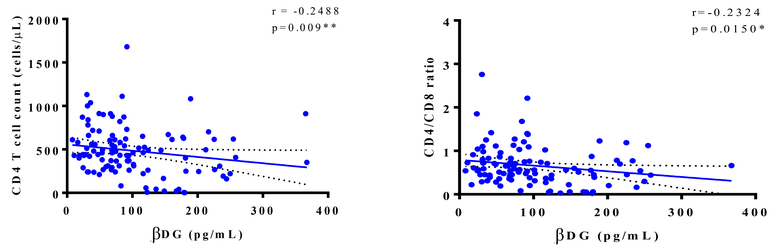
Plasma levels of βDG in different groups of persons living with HIV and controls



Correlation of plasma levels of βDG with age and with HIV viral load



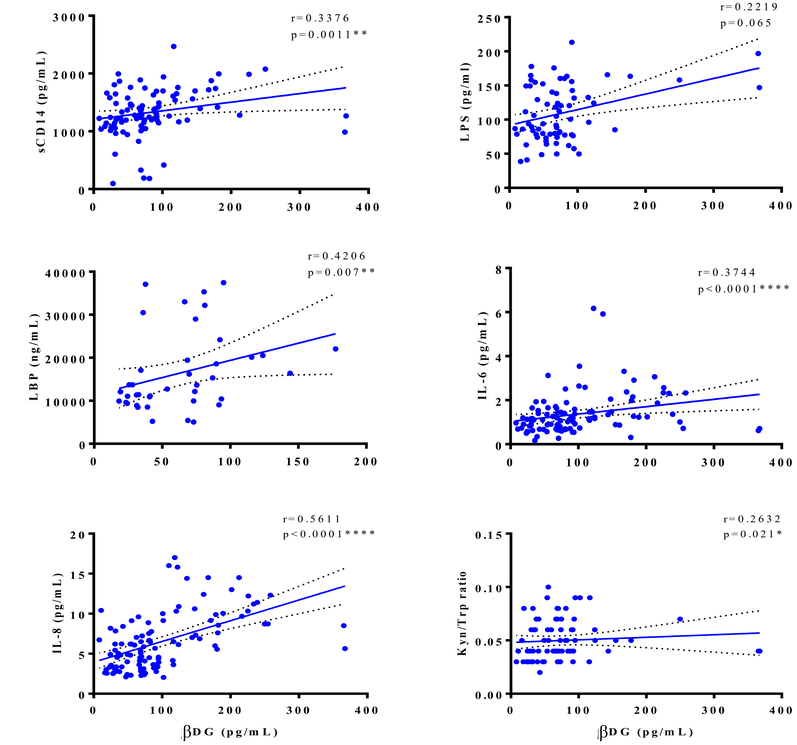
Correlation of plasma levels of βDG with CD4 T cell count and with CD4/CD8 ratio



Abbreviations and footnotes: βDG = (1→3)-β-D-glucan; IQR = Interquartile Range; VL = Viral Load; PHI = Primary HIV infection; ART- = Antiretroviral Therapy Naïve; ART+ = on ART; UCs = HIV-Uninfected Controls; *p<0.05; **p<0.01; ***p<0.001; ****p<0.00001; Note: Correlation analyses does not include UCs; n=40 for correlation of βDG with LBP; Correlation analysis of βDG with VL includes only viremic ART naïve groups; Plasma Galactomannan levels were below the cutoff among all participants.

Results

Correlation of plasma levels of βDG with markers of microbial translocation and inflammation



Conclusions

βDG is elevated during early and chronic, treated and untreated HIV infection. Elevated βDG levels correlated with the markers of disease progression, microbial translocation, and inflammation. Future studies assessing the impact of fungal translocation on AIDS-related events will help better understand the role of fungal translocation in HIV-associated systemic inflammation.

Acknowledgements

We thank the study participants for their contribution. We are grateful to Angie Massicotte, Josée Girouard and Mario Legault for study coordination and support.