Published in final edited form as:

Virus Genes. 2018 June ; 54(3): 361–367. doi:10.1007/s11262-018-1555-2.

Human pegivirus (HPgV) infection in Ghanaians co-infected with human immunodeficiency virus (HIV) and hepatitis B virus (HBV)

Kombo F. N'Guessan¹, Ceejay Boyce¹, Awewura Kwara², Timothy N. A. Archampong^{3,4}, Margaret Lartey^{3,4}, Kwamena W. Sagoe⁵, Ernest Kenu^{4,6}, Adjoa Obo-Akwa³, and Jason T. Blackard¹

¹Division of Digestive Diseases, University of Cincinnati College of Medicine, Cincinnati, Ohio

²College of Medicine and Emerging Pathogens Institute, University of Florida, Gainesville, Florida

³Department of Medicine and Therapeutics, School of Medicine and Dentistry, College of Health Sciences, University of Ghana, Accra, Ghana

⁴Korle-Bu Teaching Hospital, Accra, Ghana

⁵Department of Medical Microbiology, School of Biomedical and Allied Health Sciences, College of Health Sciences, University of Ghana, Accra, Ghana

⁶School of Public Health, College of Health Sciences, University of Ghana, Accra, Ghana

Abstract

Human pegivirus (HPgV) is a positive single-stranded RNA virus in the *Flaviviridae* family. Phylogenetic analysis reveals the presence of multiple HPgV genotypes with distinct geographic locations. HPgV is of interest because of its potential beneficial impact on HIV disease progression. Despite this, the effects of HPgV in the context of other viral infections, such as hepatitis B virus (HBV), are poorly understood, and data from resource-limited settings are scarce. Therefore, we conducted a cross-sectional analysis of HPgV in HIV/HBV co-infected patients in Ghana.

Sera from 100 HIV/HBV co-infected individuals were evaluated for HPgV RNA, and the genotype determined by sequencing the 5' untranslated region. HPgV RNA was detected in 27 samples (27%). Of these, 26 were genotyped successfully with 23 belonging to HPgV genotype 1 and 3 belonging to HPgV genotype 2. The presence of HPgV RNA had no statistically significant impact on CD4 cell count or HBV DNA titers in the HIV/HBV co-infected patients. However, there was a trend towards decreased HBV DNA levels in HPgV RNA positive patients with CD4 cell count <200 ($p = 0.0626$).

Corresponding author: Jason T. Blackard, Division of Digestive Disease, University of Cincinnati College of Medicine, Cincinnati, OH, USA, jason.blackard@uc.edu; phone: +1-513-558-4389.

Statement of author contributions

KFN, AK, TNA, and JTB designed the study. KFN, CB, AK, TNA, ML, KWS, EK, AOA, and JTB enrolled the study population, conducted laboratory work, and/or performed data analysis. All authors edited the manuscript draft.

Compliance with ethical standards

The authors declare that they have no conflicts of interests. Informed consent was obtained from individuals attending the Fevers Unit of the Korle-Bu Teaching Hospital in Accra, Ghana.

HPgV co-infection is common in Ghana. The effect of HPgV on HIV or HBV disease among HIV/HBV co-infected patients was minimal. However, decreased HBV DNA levels in HPgV RNA positive patients with low CD4 cell counts highlight the need for prospective studies of HPgV in HIV and hepatitis co-infected patients, especially in those with advanced HIV disease, to study further the effects of HPgV on liver disease.

Keywords

pegivirus (HPgV); GB virus C (GBV-C); HIV; hepatitis B virus (HBV); Ghana; Africa

Introduction

Human pegivirus (HPgV), formerly known as GB virus C (GBV-C), is a member of the *Flaviviridae* family of single-stranded, positive-sense RNA viruses and has genomic similarity to hepatitis C virus (HCV) (1, 2). Multiple studies have evaluated the possible association of HPgV with a variety of clinical diseases. A weak association between HPgV and non-Hodgkin's lymphoma has been reported recently (3), although all other studies found no causal link between HPgV and any clinical disease (1, 2). In contrast, several studies reported that HPgV infection is associated with delayed HIV disease progression as indicated by higher CD4 cell counts, lower HIV RNA levels, and/or longer disease-free survival (4–8).

Phylogenetic analysis of HPgV 5' untranslated region (UTR) has led to the identification of multiple HPgV genotypes (9, 10). Genotypes 1 and 2 are common throughout the Americas, and northern and central Africa. Genotypes 3 and 4 are present in Asia. Genotype 5 circulates within central and southern Africa. Genotype 6 has been identified in Southeast Asia, while genotype 7 has been reported only in China to date (10). Thus, HPgV diversity is extensive and could impact viral phenotype. In Western countries, up to 4% of healthy blood donors are infected with HPgV (11–13), while in the prevalence in the general population may be as high as 5% to 18% in developing countries (14–16). Among HIV-positive individuals, the prevalence of HPgV RNA ranges from 14% to 45% (17). Despite the high rates of infection, data on HPgV in resource-limited areas are limited and deserves additional consideration (18). Thus, the objective of this study was to determine the prevalence of HPgV in HIV/HBV co-infected patients from Ghana and evaluate the potential consequences of HPgV infection on HIV and HBV disease outcomes.

Materials and Methods

Study participants

This was a secondary analysis of a previous study of HIV/HBV co-infected patients were collected at the Fevers Unit of the Korle-Bu Teaching Hospital in Accra, Ghana (19). Following informed consent, adult HIV patients attending the Fevers Unit between 2012 and 2014 were screened for HBsAg using the qualitative Core HBsAg rapid test (Core Diagnostics, Birmingham, UK). Of note, all HIV-infected patients on ART in Ghana would have received a 3TC-containing regimen irrespective of the degree of severity of HIV

disease or HBV status. Hepatitis C virus status was not determined in this cohort; however, a previous study in HIV-positive individuals from the same medical center reported that HCV seropositivity was low and did not impact CD4 cell count or HIV viral load (20). Plasma HBV DNA levels were determined using fully automated COBAS® TaqMan® Analyzer (Roche Diagnostics GmbH, Mannheim, Germany). The lower limit of detection of the Roche TaqMan assay was 20 IU/mL with a linear range from 20 to 170,000,000 IU/mL. Additional laboratory tests such as CD4 cell counts were obtained from patients. The University of Ghana Medical School, Accra, Ghana and Lifespan Hospital, Providence, Rhode Island Institutional Review Boards approved the study. For the currently analysis, HIV/HBV co-infected individuals with the HBV viral loads >400 IU/mL were evaluated to explore the potential association between HPgV status and HBV infection/HBV viral load.

Detection of HPgV and classification of HPgV genotype

Viral RNA was extracted using the QIAmp Ultrasens Virus Kit (for DNA and RNA) (QIAGEN, Valencia, CA). As described previously (21–23), HPgV RNA was detected by amplification of the 5' untranslated region (UTR) with the antisense primer 5' – ATG CCA CCC GCC CTC ACC CGA A – 3' (nucleotides [nt] 494–473 according to GenBank accession number AY196904) and the sense primer 5' – AAA GGT GGT GGA TGG GTG ATG – 3' (nt 67–87) via OneStep RT-PCR (QIAGEN). Amplification conditions were 50°C for 59 min, 10 min at 94°C, then 35 cycles of 30 s at 94°C, 1 min at 55°C, and 1 min at 72°C, followed by 20 min at 72°C. First-round PCR products were used in nested PCR with the antisense primer 5' – CCC CAC TGG TCY TTG YCA ACT C – 3' (nt 362–341) and sense primer 5' – AAT CCC GGT CAY AYT GGT AGC CAC T – 3' (nt 107–131). After 35 cycles of 30 sec at 94°C, 30 sec at 55°C, and 1 min at 72°C, a 256 nt PCR product was visualized by agarose gel electrophoresis. Population-based sequencing of amplicons was performed, and 5' UTR sequences were aligned with GenBank accession numbers U59540, U59543, U59549, and U59555 (genotype 1); HGU59518, D90600, HGU59534, and HGU59535 (genotype 2); U59538 and U59539 (genotype 3); AB018667 and AB021287 (genotype 4); AY949771, AF092894, LT009490, and KC618401 (genotype 5); AB003292 and AF177619 (genotype 6); and HQ331234 and HQ331235 (genotype 7). Phylogenetic inference was performed using a Bayesian Markov chain Monte Carlo (MCMC) approach executed in the Bayesian Evolutionary Analysis by Sampling Trees version 1.8.4 (24) with an uncorrelated log-normal relaxed molecular clock, generalized time reversible model, and nucleotide site heterogeneity estimated with a gamma distribution. The MCMC analysis was run for a chain length of 500,000,000. All effective sample sizes were >250 indicating sufficient sampling. The maximum clade credibility tree was selected from the posterior tree distribution after a 10% burn-in using TreeAnnotator version 1.8.4. HPgV sequences are available in GenBank through the accession numbers MG229645 – MG229670.

Statistical analysis

Sociodemographic and clinical data available at baseline were evaluated using the Chi-squared or Mann-Whitney tests using PRISM version 6.03 and SigmaPlot version 12.

Results

100 HIV/HBV co-infected individuals – including 57 patients who were antiretroviral (ART)-naïve and 43 patients who had received at least 9 months of 3TC-containing ART – were evaluated for the presence of HPgV. Of these, HPgV RNA was detected in 27 samples (27%). Patients with HPgV did not differ from those that were HPgV negative with respect to age, gender, or alanine aminotransferase levels (Table 1). HPgV positivity was 19.3% and 37.2% in the ART naïve and ART experienced groups, respectively. Of the HPgV positive samples, genotyping was determined by phylogenetic analysis of the 5'UTR for 26 samples (Figure 1). Genotypes present included 23 with genotype 1 (88.5%) and 3 with genotype 2 (11.5%).

As discussed above, HPgV viremia has been associated with increased CD4 counts, reduced HIV viral loads, and slower disease progression in some studies (4–8). However, the impact of HPgV infection on other viral co-infections is less clear. Thus, we evaluated differences in CD4 T cell count between HPgV positive and negative individuals. HPgV status did not have a significant impact on CD4 cell count or HBV DNA level in the full cohort (Figure 2A). However, stratification of HIV/HBV co-infected individuals by ART status showed that CD4 cell counts were higher for ART experienced individuals who were also HPgV positive compared to ART experienced individuals who were HPgV negative (860 versus 80; $p = 0.049$). This difference in CD4 cell count was not significant in the ART naïve individuals (523 versus 382; $p = 0.76$). There was no statistical difference in plasma HIV RNA levels by HPgV status ($p = 0.428$) (Figure 2B), and the percentage of undetectable HIV RNA was 26.0% and 25.9% for HPgV positive and HPgV negative individuals, respectively.

Given the negative effects of HIV infection on the natural history of HBV, we also evaluated the effects of HPgV infection on HBV DNA levels. When including all HIV/HBV co-infected individuals regardless of CD4 cell count, there was no statistically significant difference in HBV DNA levels between HPgV positive and negative patients (median = 6.505 and 6.662 $\log_{10}$ copies/mL; $p = 0.932$) (Figure 3). Similarly, ART status did not have a significant impact on HBV DNA levels between HPgV positive and negative patients (data not shown). In contrast, a trend towards lower HBV DNA levels was observed in HPgV positive patients with CD4 T cell counts < 200 cells/ μ L ($p = 0.0626$). We previously evaluated HBV genotypes in this population and found that 92.1% had HBV genotype E with remaining belonging to genotype A or D (25).

Discussion

Population-based studies of HPgV have been conducted in only 13 sub-Saharan African countries to date (18). Six studies of HPgV have been conducted in Ghana, although only two were prevalence studies that included HIV positive individuals (26, 27); none included HIV/HBV co-infected individuals. The prevalence of HPgV in blood donor populations and pregnant women in Ghana is 4% – 13.5% and 21.7% – 26.1%, respectively. Others have reported HPgV positivity rates of 16.2% – 20% among HIV-positive Ghanaians (26, 27). A recent meta-analysis, reported that HBV co-infection rates were 2.4% – 41.7 % (pooled prevalence rate of 13.6 %) in HIV-positive Ghanaians. Thus, the current study focused on

this understudied and difficult-to-manage patient population. We report an HPgV prevalence of 27% in HIV/HBV co-infected individuals in Ghana, higher than the prevalence of the virus in HBV-negative HIV patients. These results are expected given the common routes of transmission shared by all three viruses – sexual contact, exposure to blood, and less frequently from mother to child.

HPgV genotype diversity may impact HIV disease progression. For instance, Muerhoff *et al.* reported that CD4 cell counts were lower in HIV-positive patients co-infected with HPgV genotype 2a compared to those with HPgV genotype 2b (28). In the United States and Brazil, higher CD4 cell counts were associated with HPgV genotype 2 compared to genotype 1, although no difference was reported in Australia (21, 29, 30). To date, the predominant HPgV genotype circulating in West Africa has been identified as genotype 1 (18). Our study confirms this finding but highlights the presence of genotype 2 as well.

It is well documented that HIV co-infection has a significant impact on the natural history of HBV resulting in decreased immune responses and increased HBV transmission (31–34). HIV further contributes to increased rates of HBV chronicity, enhanced HBV replication, and accelerated liver-related morbidity and mortality (reviewed in (35)). Conflicting results have been found on the effect of HBV on HIV disease progression. HBV may lead to higher baseline HIV viral loads, lower CD4 cell counts, and increased mortality in HIV/HBV co-infected participants compared with HIV mono-infected individuals, although this has not been observed in all studies (36–41). Interestingly, in the current study, there was a trend of lower HBV DNA levels in HPgV positive patients with CD4 cell counts < 200 cells/ μ L.

Limitations to the current study should be noted. First, the population size is modest, and all patients were enrolled in a single tertiary referral center in Accra. Thus, results may not be generalizable to other regions of the country or to HIV-negative individuals. Secondly, HIV viral loads are only available for treatment-experienced individuals; therefore, a robust comparison of HIV viral loads by HPgV status is not possible in all individuals. Despite these limitations, the finding of decreased HBV DNA levels in HPgV RNA positive patients with low CD4 cell counts is intriguing and highlights the need for additional studies of complex virus-virus interactions. In addition, CD4 cell count was higher in ART-experienced patients who were HPgV positive compared to those who were HPgV negative. Third, as with most studies to date, there is no information regarding the mode of HPgV transmission or the timing of infection. Fourth, HPgV RNA is a sign of current infection, although HPgV clearance does occur. We and others have demonstrated that the majority of HIV-infected individuals who clear HPgV viremia fail to develop detectable E2 antibodies (21, 42). Thus, E2 antibodies are not a reliable marker of previous HPgV infection in immunocompromised individuals. Fifth, additional study groups such as HBV mono-infection were not included, largely due to the parent study design; however, there are no data showing that HPgV and HBV interact directly in the absence of HIV. Sixth, this is a cross-sectional study; thus, data on incident HPgV infections or cleared infections are not available and information on the evolution of HIV or liver disease in the presence/absence of HPgV infection is lacking, although this clearly represents an important next step in our understanding of HPgV/HIV/HBV interactions.

Given the high prevalence of HPgV in many resource-limited settings, evaluating its impact on other common viral co-infections is important. While no impact of HPgV infection on HIV viral load or CD4 cell counts were noted, the small sample size may limit power to detect such differences. The finding of lower HBV DNA levels in HIV/HBV co-infected individuals with HPgV infection is intriguing given that the major impact of HPgV on HIV occurs during late HIV disease (43). Thus, this finding requires additional investigation to determine the impact of HPgV on HBV-related disease processes in larger cohorts with a wide range of CD4 cell counts.

Acknowledgments

The authors would like to thank the study participants of the Fevers Unit of the Korle-Bu Teaching Hospital in Accra, Ghana, and the Pathobiology & Molecular Medicine PhD program at the University of Cincinnati College of Medicine for their generous support. This study was funded by a 2012 International Developmental Grant from the Lifespan/Tufts/Brown CFAR (P30AI042853) and the Brown/Tufts AIDS International Training and Research Program (D43TW000237) to Drs. Archampong and Kwara. Additional support was provided by Brown University – University of Ghana partnership through a USAID/HED grant (Award # AEG-A-00-05-00007).

References

1. Bhattarai N, Stapleton J. Trends in Microbiology. 2012; 20:124–130. [PubMed: 22325031]
2. Stapleton J. Seminars in Liver Disease. 2003; 23:137–148. [PubMed: 12800067]
3. Chang CM, Stapleton JT, Klinzman D, McLinden JH, Purdue MP, Katki HA, Engels E. Cancer Research. 2014; 74:5553–5560. [PubMed: 25115299]
4. Xiang J, Wunschmann S, Diekema DJ, Klinzman D, Patrick KD, George SL, Stapleton J. New England Journal of Medicine. 2001; 345:707–714. [PubMed: 11547739]
5. Williams CF, Klinzman D, Yamashita TE, Xiang J, Polgreen PM, Rinaldo C, Liu C, Phair J, Margolick JB, Zdunek D, Hess G, Stapleton J. New England Journal of Medicine. 2004; 350:981–990. [PubMed: 14999110]
6. Tillmann H, Heiken H, Knapik-Botor A, Heringlake S, Ockenga J, Wilber J, Goergen B, Detmer J, McMorro M, Stoll M, Schmidt R, Manns M. New England Journal of Medicine. 2001; 345:715–724. [PubMed: 11547740]
7. Lefrere JJ, Roudot-Thoraval F, Morand-Joubert L, Petit JC, Lerable J, Thauvin M, Mariotti M. Journal of Infectious Diseases. 1999; 179:783–789. [PubMed: 10068572]
8. Heringlake S, Ockenga J, Tillmann HL, Trautwein C, Meissner D, Stoll M, Hunt J, Jou C, Solomon N, Schmidt RE, Manns M. Journal of Infectious Diseases. 1998; 177:1723–1726. [PubMed: 9607857]
9. Muerhoff AS, Dawson GJ, Desai S. Journal of Medical Virology. 2006; 78:105–111. [PubMed: 16299729]
10. Feng Y, Zhao W, Feng Y, Dai J, Li Z, Zhang X, Liu L, Bai J, Zhang H, Lu L, Xia X. PLoS One. 2011; 6:e21151. [PubMed: 21998624]
11. Dawson GJ, Schlauder GG, Pilot-Matias TJ, Thiele D, Leary TP, Murphy P, Rosenblatt JE, Simons JN, Martinson FE, Gutierrez RA, Lentino JR, Pachucki C, Muerhoff AS, Widell A, Tegtmeier G, Desai S, Mushahwar I. Journal of Medical Virology. 1996; 50:97–103. [PubMed: 8890047]
12. Hyland CA, Mison L, Solomon N, Cockerill J, Wang L, Hunt J, Selvey LA, Faoagali J, Cooksley WG, Young IF, Trowbridge R, Borthwick I, Gowans E. Transfusion. 1998; 38:821–827. [PubMed: 9738621]
13. Blair CS, Davidson F, Lycett C, McDonald DM, Haydon GH, Yap PL, Hayes PC, Simmonds P, Gillon J. Journal of Infectious Diseases. 1998; 178:1779–1782. [PubMed: 9815233]
14. Bassit L, Kleter B, Ribeiro-dos-Santos G, Maertens G, Sabino E, Chamone D, Quint W, Sáez-Alquézar A. Vox Sanguinis. 1998; 74:83–87. [PubMed: 9501405]
15. Ren FR, Wang Y, Li H, Chen HS, Zhao H. Vox Sanguinis. 1998; 74:51–52. [PubMed: 9481862]

16. Akiyama H, Nakamura N, Tanikawa S, Sakamaki H, Onozawa Y, Shibayama T, Tanaka S, Tsuda F, Okamoto H, Miyakawa Y, Mayumi M. Bone Marrow Transplantation. 1998; 21:1131–1135. [PubMed: 9645576]
17. Berzsenyi MD, Bowden DS, Roberts S. Journal of Clinical Virology. 2005; 33:257–266. [PubMed: 15922655]
18. Singh S, Blackard J. Reviews in Medical Virology. 2017; 27:1951.
19. Archampong TN, Lartey M, Sagoe KW, Obo-Akwa A, Kenu E, Gillani FS, Yang H, Boamah I, Flanigan T, Kwara A. BMC Infectious Diseases. 2016; 16:14. [PubMed: 26759172]
20. Sagoe KW, Agyei AA, Ziga F, Lartey M, Adiku TK, Seshi M, Arens MQ, Mingle J. Journal of Medical Virology. 2012; 84:6–10. [PubMed: 22095533]
21. Schwarze-Zander C, Blackard JT, Zheng H, Addo MM, Lin W, Robbins GK, Sherman KE, Zdunek D, Hess G, Chung R, for, the, AIDS, Clinical, Trial, Group, A5071, Study, and Team. Journal of Infectious Diseases. 2006; 194:410–419. [PubMed: 16845623]
22. Blackard JT, Ma G, Welge JA, King CC, Taylor LE, Mayer KH, Klein RS, Celentano DD, Sobel JD, Jamieson DJ, Gardner L. PLoS One. 2014; 9:e114467. [PubMed: 25493916]
23. N'Guessan KF, Anderson M, Phinius B, Moyo S, Malick A, Mbangiwa T, Choga WT, Makhema J, Marlink R, Essex M, Musonda R, Gaseitsiwe S, Blackard J. Open Forum Infectious Diseases. 2017; 4:ifx222.
24. Drummond AJ, Suchard MA, Xie D, Rambaut A. Molecular Biology and Evolution. 2012; 29:1969–1973. [PubMed: 22367748]
25. Archampong TN, Boyce CL, Lartey M, Sagoe KW, Obo-Akwa A, Kenu E, Blackard JT, Kwara A. Antiviral Therapy. 2016; 2017:1.
26. Saito T, Ishikawa KI, Osei-Kwasi M, Kaneko T, Brandful JA, Nuvor V, Aidoo S, Ampofo W, Apeagyei FA, Ansah JE, Adu-Sarkodie Y, Nkrumah FK, Abe K. Hepatology Research. 1999; 13:221–231.
27. Compston LI, Li C, Sarkodie F, Owusu-Ofori S, Opare-Sem O, Allain J. Journal of Medical Virology. 2009; 81:1860–1868. [PubMed: 19774687]
28. Muerhoff AS, Tillmann HL, Manns MP, Dawson GJ, Desai S. Journal of Medical Virology. 2003; 70:141–149. [PubMed: 12629656]
29. Berzsenyi MD, Bowden DS, Roberts SK, Revill P. Journal of Gastroenterology and Hepatology. 2009; 24:1407–1410. [PubMed: 19702909]
30. Alcalde R, Nishiya A, Casseb J, Inocêncio L, Fonseca LA, Duarte A. Virus Research. 2010; 151:148–152. [PubMed: 20420864]
31. McGovern B. Antiviral Therapy. 2007; 12:H3–H13. [PubMed: 18284178]
32. Bodsworth N, Donovan B, Nightingale B. Journal of Infectious Diseases. 1989; 160:577–582. [PubMed: 2571646]
33. Colin JF, Cazals-Hatem D, Lioriot MA, Martinot-Peignoux M, Pham BN, Auperin A, Degott C, Benhamou JP, Erlinger S, Valla D, Marcellin P. Hepatology. 1999; 29:1306–1310. [PubMed: 10094979]
34. Gilson RJ, Hawkins AE, Beecham MR, Ross E, Waite J, Briggs M, McNally T, Kelly GE, Tedder RS, Weller I. AIDS. 1997; 11:597–606. [PubMed: 9108941]
35. Thio C. Hepatology. 2009; 49:S138–S145. [PubMed: 19399813]
36. Thio CL, Smeaton L, Saulynas M, Hwang H, Saravanan S, Kulkarni S, Hakim J, Nyirenda M, Iqbal HS, Laloo UG, Mehta AS, Hollabaugh K, Campbell TB, Lockman S, Currier J. AIDS. 2013; 27:191–200. [PubMed: 23032418]
37. Ladep NG, Agaba PA, Agbaji O, Muazu A, Ugoagwu P, Imade G, Cooke G, McCormack S, Taylor-Robinson SD, Idoko J, Kanki P. World Journal of Gastroenterology. 2013; 19:1602–1610. [PubMed: 23538773]
38. Attia KA, Eholié S, Messou E, Danel C, Polneau S, Chenal H, Toni T, Mbamy M, Seyler C, Wakasugi N, N'dri-Yoman T, and Anglaret X., 40 7, 2012.
39. Matthews GV, Manzini P, Hu Z, Khabo P, Maja P, Matchaba G, Sangweni P, Metcalf J, Pool N, Orsega SS, Orsega E, team P.I.s. AIDS. 2011; 25:1727–1735. [PubMed: 21716078]
40. Harania RS, Karuru J, Nelson M, Stebbing J. AIDS. 2008; 22:1221–1222. [PubMed: 18525268]

41. Hawkins C, Christian B, Ye J, Nagu T, Aris E, Chalamilla G, Spiegelman D, Mugusi F, Mehta S, Fawzi W. *AIDS*. 2013; 27:919–927. [PubMed: 23196935]
42. Berzsenyi MD, Bowden DS, Kelly HA, Watson KM, Mijch AM, Hammond RA, Crowe SM, Roberts S. *Gastroenterology*. 2007; 133:1821–1830. [PubMed: 18054555]
43. Zhang W, Chaloner K, Tillmann HL, Williams CF, Stapleton J. *HIV Medicine*. 2006; 7:173–180. [PubMed: 16494631]

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Figure 2.

A. CD4⁺ T-cell counts are shown for HPgV-positive and HPgV-negative individuals. Closed circles represent outliers. P-values are shown for the Wilcoxon Rank Sum test.

B. Plasma HIV RNA levels are shown for HPgV-positive and HPgV-negative individuals. P-values are shown for the Wilcoxon Rank Sum test.

Figure 3.

Baseline HBV viral loads (log₁₀ copies/mL) for all individuals (**A**) based on HPgV status, for individuals with CD4 cell counts <200 (**B**) and for individuals with CD4 cell counts ≥200 (**C**). Closed circles represent outliers. P-values are shown for the Wilcoxon Rank Sum test.

Table 1

Sociodemographic and clinical characteristics of HPgV-positive and HPgV-negative Ghanaians with HIV/HBV co-infection. Comparisons are made between the HPgV-positive and HPgV-negative groups using the Kruskal-Wallis test from Wilcoxon Score with the exception of male gender (chi-squared test used).

	HPgV negative (n = 73)	HPgV positive (n = 27)	P-value
Gender			
Male (n = 48)	38	10	0.27
Female (n = 52)	35	17	
Age			
<40 years (n = 53)	39	14	0.93
40 years (n = 47)	34	13	
Alanine aminotransferase (IU/L)	36.0	36.0	0.71
Median CD4 cell count (cells/mL)	320	323	0.78
Median baseline HBV DNA (IU/mL)	6.505	6.662	0.93
Patients with CD4 <200	5.237	7.782	0.06
Patients with CD4 ≥ 200	6.865	6.109	0.20