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Prevalence of HIV/hepatitis B and HIV/hepatitis C coinfection among people of East, South, Central and West African ancestry in the United Kingdom

Running title: HIV and HBV/HCV coinfection in Africans

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Abstract

Regional variability in the prevalence of hepatitis B (HBV) and C (HCV) is reported in sub-Saharan Africa, although data for people with HIV are sparse. We determined the prevalence of HBV/HCV in 2,473 people of African ancestry with HIV in the UK. Overall, 6.2% were co-infected with HBV and 1.3% with HCV. Central (aOR 2.40 [95%CI 1.23-4.67] and West (2.10 [1.29-3.41]) African ancestry was associated with HBV and Central (6.98 [2.00-24.43]) African ancestry with HCV.

Key words: Hepatitis, HIV, Africa, HBV, HCV, HDV, epidemiology, diaspora

Chronic hepatitis B (HBV) and C (HCV) are a major cause of cirrhosis, hepatocellular carcinoma in sub-Saharan Africa [1]. An estimated 10-15% of people with HIV (PWH) in sub-Saharan Africa are co-infected with HBV and some 5-7% may be co-infected with HCV, although several studies across all regions report substantially lower prevalence rates [2-4]. Data on hepatitis D (HDV) coinfection in people with HIV/HBV are limited to relatively small cohort studies and range from 0-5% in East/South Africa to 2-25% in West/Central Africa [5, 6]. However, substantial heterogeneity in survey participant characteristics and methodology limit the direct comparison of prevalence estimates across African regions. We sought to compare the prevalence of HBV, HCV and HDV and the variation in HBV and HCV genotypes in a large cohort of people with HIV (PWH) originating from sub-Saharan Africa in the United Kingdom.

The GEN-AFRICA study enrolled black PWH aged >18 years at 15 HIV clinics across England between May 2018 and February 2020; analyses were restricted to individuals whose mother and father were born in the same region of sub-Saharan Africa. Viral hepatitis status (HBsAg, anti-HBc, anti-HCV, HCV RNA [if anti-HCV positive] and anti-HDV if HBsAg positive], and HBV/HCV genotype were ascertained; HBV was defined by positive HBsAg and HCV by anti-HCV status. Characteristics were described and compared using chi squared tests for categorical variables, and Kruskal-Wallis tests or ANOVA for continuous variables, as appropriate (Table S1/S2, http://links.lww.com/QAD/C129). Logistic regression was used to analyse the association between region of ancestry and HBV/HCV.

Of the 3,026 participants enrolled in the GEN-AFRICA study, 2,468 (81.6%) reported East, South, Central or West African ancestry and were included in the analyses (Fig S1, http://links.lww.com/QAD/C129). The demographic and clinical characteristics of these participants are shown in Table 1. Participants were predominantly women with longstanding and well-controlled HIV infection on ART which in over half included tenofovir.

Hepatitis B and D

The overall prevalence of HBsAg was 6.2%, ranging from 4.1-4.4%, 8.5% and 10.2% in those of East/South, West and Central African ancestry. At country level, the prevalence of HBsAg exceeded 10% in participants from Cameroon, Ghana, Sierra Leone, Guinea, and Guinea Bissau (Fig S2, http://links.lww.com/QAD/C129 and Table S3, http://links.lww.com/QAD/C129). The overall prevalence of anti-HBc was 49.4%, and as for HBsAg, the highest anti-HBc prevalence was observed in those of West and Central African ancestry. The predominant HBV genotype was A in East/South Africans and E in West Africans. Among those with HBsAg who were tested for anti-HDV, the overall prevalence of HDV co-infection was 5.2%. HBV was associated with gender, West/Central African ancestry, nadir CD4 cell count, and exposure to tenofovir. In multivariable analysis, women remained at substantially lower odds (0.50 [95%CI 0.35, 0.71], and those of West and Central African ancestry at more than two-fold greater odds of HBV (2.10 [1.29-3.41] and (2.40 [1.23, 4.67], respectively) (Table S4, http://links.lww.com/QAD/C129).

Hepatitis C

The overall prevalence of anti-HCV and HCV RNA was 1.3% and 0.17%, respectively. The highest prevalence of HCV was observed among those of Central African ancestry. The overall distribution of HCV genotypes, where available, varied, and did not map to an exact geographic region, although only a small number of HCV genotypes were available for analysis (Table 1). HCV was associated with Central African ancestry and sex between men. In multivariable analysis, Central African ancestry remained associated with HCV (6.98 [2.00, 24.43] overall; 12.5 [1.4-113.7] among male participants) (Table S4, http://links.lww.com/QAD/C129). For both HBV and HCV, similar results were obtained in sensitivity analyses that excluded participants with stage 5 CKD (Table S5, http://links.lww.com/QAD/C129).

Two systematic reviews that reported HIV/HBV co-infection rates by region have yielded similar, albeit slightly higher estimates to ours (about 5% in East/South Africa and 10-15% in West Africa) [2, 4]. The authors noted the lack of good quality prevalence data for HIV/HBV coinfection for many countries beyond Nigeria and South Africa and potential for publication bias, with many of the studies performed in specific populations (e.g. adolescents, children or pregnant women) [2]. Possible explanations for the slightly higher rates of HBV co-infection in studies performed in Africa might include differences in participant (e.g. age and gender [7]), HIV (e.g. CD4 cell count and HIV viral load), HBV replicative status (e.g. prevalence of pre-core and basal core promoter mutations [8]), or access to tenofovir-based ART [9].

We found that the prevalence of HBV coinfection in West/Central Africa was approximately two-fold higher than in East/South Africa. The highest prevalence of both HBsAg and anti-HBc was observed in people of West/Central African ancestry may indicate a higher background prevalence of neonatal- and childhood-acquired HBV in West/Central Africa and hence higher rates of persistent infection. The mean age of 48 years suggests that most participants were born in Africa prior to the institution of universal HBV vaccination programmes, and before widespread HIV transmission. Thus, persistent HBV infections were likely acquired in infancy and HIV by later heterosexual transmission in most participants. However, we cannot rule out the possibility of simultaneous mother to child or parenteral transmission of HIV and HBV in younger individuals.

We report that, except for Central Africa, the prevalence of HCV was generally around 1%, which is similar to the WHO estimate for the African region [1]. The spectrum of HCV genotypes in our cohort is consistent with recent data for HCV mono-infected individuals of African ancestry [10]. It is thought that parenteral exposure through (non-medical) circumcision and scarification and poor medical practice (non-sterile equipment) are an important source of HCV acquisition in sub-Saharan Africa.

In summary, our study provides robust estimates of, and regional variability in HBV/HCV prevalence in people of African ancestry with HIV. These data support the scale up of HBV

screening, vaccination and prevention of mother-to-child transmission programmes, testing for HCV and HDV, and tenofovir-based ART in sub-Saharan Africa and for members of the African diaspora. Use of non-tenofovir ART regimens should be restricted to settings where HBsAg can be ruled out.

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The study was designed by KC and FAP. NP, KC and FAP performed the literature review. JF, CC, SLP, FB, AU, MR and FAP were site principal investigators and coordinated recruitment, sample and data collection at their sites. RH and FAP performed the analyses. RH, NP, GD, KC and FAP wrote the first draft of the manuscript with input from SB. All authors revised and approved the final version of the manuscript. The authors would like to thank the participants and members of the GEN-AFRICA study group (appendix, http://links.lww.com/QAD/C129).

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Conflict of Interest Statement

JF reports grant funding from Gilead. AU reports personal feed from Janssen, Gilead, MSD and ViiV. SB reports grants and/or personal fees from Gilead Sciences, Janssen, MSD, Roche and ViiV. GD reports grants from Abbott, personal fees from Gilead and Arbutus (donated to a registered charity), and personal fees for membership of a Drug Safety Monitoring Board from Enanta, Janssen, Glaxo Smith Kline and Aligos. FAP reports grants and/or personal fees from Gilead Sciences, ViiV, Janssen, and MSD. All others report no conflicts of interest.

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Table 1 Demographic and clinical characteristics of the study participants and details of hepatitis B, C and D co-infection status. Participants are stratified by African region of ancestry.

		Total	East	South	Central	West	p-value
		N=2,468	N=585	N=810	N=168	N=905	
Age, years	Mean (SD)	48.1 (9.8)	49.1 (9.7)	48.3 (9.9)	47.8 (10.2)	47.2 (9.8)	0.002
Sex (female)	n (%)	1,531 (62.0)	377 (64.4)	562 (69.4)	95 (56.5)	497 (54.9)	<0.001
HIV Risk							<0.001
Heterosexual	n (%)	2,150 (87.1)	484 (82.7)	724 (89.4)	151 (89.9)	791 (87.4)	
MSM	n (%)	32 (1.3)	8 (1.4)	7 (0.9)	0 (0.0)	17 (1.9)	
Vertical	n (%)	107 (4.3)	26 (4.4)	37 (4.6)	5 (3.0)	39 (4.3)	
IVDU/Blood products	n (%)	20 (0.8)	4 (0.7)	3 (0.4)	1 (0.6)	12 (1.3)	
Unknown	n (%)	159 (6.4)	63 (10.8)	39 (4.8)	11 (6.5)	46 (5.1)	
Time since HIV diagnosis, years	Mean (SD)	14.1 (6.3)	16.6 (7.2)	14.9 (5.3)	14.5 (6.3)	11.5 (5.6)	<0.001
Prior AIDS	n (%)						
Nadir CD4 count (cells/mm^3)	Median (IQR)	194 (78-329)	182 (80-319)	200 (85-335)	181.5 (47-302)	196 (76-351)	0.21
Current CD4 count (cells/mm^3)	Median (IQR)	551 (396-719)	534 (376-706)	599 (430-763)	511 (355-645)	531 (390-705)	<0.001
On ART	n (%)	2,444 (99.0)	581 (99.3)	806 (99.5)	167 (99.4)	890 (98.3)	0.07
Tenofovir-containing regimen	n (%)	1,432 (58.0)	337 (57.6)	493 (60.9)	107 (63.7)	495 (54.7)	0.03
HIV RNA <200 copies/mL	n (%)	2,302 (93.3)	553 (94.5)	766 (94.6)	152 (90.5)	831 (91.8)	0.03

HBsAg positive	n/N (%)	151/2,433 (6.2)	25/573 (4.4)	33/796 (4.1)	17/150 (10.2)	76/897 (8.5)	<0.001
Anti-HBc positive	n/N (%)	1,141/2,308 (49.4)	247/543 (45.5)	312/739 (42.2)	95/162 (58.6)	487/864 (56.4)	<0.001
HBsAg positive/anti-HBc positive	n/N (%)	151/1,144 (13.2)	25/247 (10.1)	33/312 (10.6)	17/95 (17.9)	76/487 (15.6)	0.04
HBsAg negative/anti-HBc positive	n/N (%)	990/1,144 (86.5)	222/247 (89.9)	279/312 (89.4)	78/95 (82.1)	411/487 (84.4)	
HBV Genotype							
HBV Genotype A	n/N (%)	11/42 (26.2)	4/6 (66.7)	5/5 (100)	1/2 (50.0)	1/29 (3.4)	
HBV Genotype D	n/N (%)	1/42 (2.4)	1/6 (16.7)	0 (0)	0 (0)	0 (0)	
HBV Genotype E	n/N (%)	30/42 (71.4)	1/6 (16.7)	0 (0)	1/2 (50.0)	28/29 (96.6)	
Anti-HDV positive	n/N (%)	6/115 (5.2)	0/19 (0.0)	1/21 (4.8)	2/12 (16.7)	3/63 (4.8)	0.24
HCV (anti-HCV)	n (%)	30/2,399 (1.3)	4/569 (0.7)	9/773 (1.2)	7/156 (4.3)	10/871 (1.1)	0.003
HCV Genotype 1	n/N (%)	6/17 (35.3)	0 (0)	2/2 (100)	2/7 (28.6)	2/6 (33.3)	
HCV Genotype 2	n/N (%)	3/17 (17.6)	0 (0)	0 (0)	1/7 (14.3)	2/6 (33.3)	
HCV Genotype 4	n/N (%)	7/17 (41.2)	1/2 (50.0)	0 (0)	4/7 (57.1)	2/6 (33.3)	
HCV Genotype 5	n/N (%)	1/17 (5.9)	1/2 (50.0)	0 (0)	0 (0)	0 (0)	

MSM=men who have sex with men; IVDU=intravenous drug use; ART=antiretroviral therapy; HBsAg=hepatitis B surface antigen;

anti-HBc=hepatitis B core IgG antibody; HBV=hepatitis B; HDV=hepatitis D (delta); HCV=hepatitis C; SD=standard deviation; IQR=inter-quartile range