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Role of unsafe medical practices and sexual behaviours in the hepatitis B and C syndemic and HIV co-infection in Rwanda: a cross-sectional study

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ABSTRACT

Objectives This study describes the burden of the hepatitis B, C and HIV co-infections and assesses associated risk factors.

Setting This analysis used data from a viral hepatitis screening campaign conducted in six districts in Rwanda from April to May 2019. Ten health centres per district were selected according to population size and distance.

Participants The campaign collected information from 156 499 participants (51 496 males and 104 953 females) on sociodemographic, clinical and behavioural characteristics. People who were not Rwandan by nationality or under 15 years old were excluded.

Primary and secondary outcomes The outcomes of interest included chronic hepatitis C virus (HCV) infection, chronic hepatitis B virus (HBV) infection, HIV infection, co-infection HIV/HBV, co-infection HIV/HCV, co-infection HBV/HCV and co-infection HCV/HBV/HIV. Multivariable logistic regressions were used to assess factors associated with HBV, HCV and HIV, mono and co-infections.

Results Of 156 499 individuals screened, 3465 (2.2%) were hepatitis B surface antigen positive and 83% (2872/3465) of them had detectable HBV desoxy-nucleic acid (HBV DNA). A total of 4382 (2.8%) individuals were positive for antibody-HCV (anti-HCV) and 3163 (72.2%) had detectable HCV ribo-nucleic acid (RNA). Overall, 36 (0.02%) had HBV/HCV co-infection, 153 (0.1%) HBV/HIV co-infection, 238 (0.15%) HCV/HIV co-infection and 3 (0.002%) had triple infection. Scarification or receiving an operation from traditional healer was associated with all infections. Healthcare risk factors—history of surgery or transfusion—were associated with higher likelihood of HIV infection with OR 1.42 (95% CI 1.21 to 1.66) and OR 1.48 (1.29 to 1.70), respectively, while history of physical traumatic assault was associated with a higher likelihood of HIV and HBV/HIV co-infections with OR 1.69 (95% CI 1.51 to 1.88) and OR 1.82 (1.08 to 3.05), respectively.

Conclusions Overall, mono-infections were common and there were differences in significant risk factors associated with various infections. These findings highlight the magnitude of co-infections and differences in underlying risk factors that are important for designing prevention and care programmes.

Strengths and limitations of this study

- ► This study used serological markers and molecular tests for hepatitis C virus (HCV) and hepatitis B virus (HBV) testing to assess the burden of HBV, HCV and HIV infections among the general population in a developing country.
- ► Although various risk factors were assessed, information on substance use was not available.
- ► Participants were from only six districts. Therefore, the prevalence estimates and risk factors found to be associated with HCV, HBV, HIV and their co-infections may not be generalisable to the entire population.

BACKGROUND

Globally, hepatitis B and C virus infections are among the leading causes of mortality with about 1 400 000 attributable deaths every year.[1] Despite substantial improvements in HIV antiretroviral treatment roll-out, new HIV infections and HIV/AIDS-related deaths remain high, with 1.7 million new HIV infections and about 770 000 deaths in 2018 worldwide.[2] Globally, 5%–20% of people living with HIV (PLHIV) are co-infected with HBV, though rates of chronic HBV in HIV-infected individuals vary significantly across regions and risk groups.[3] Similarly, 6.2% (2 278 400) of all PLHIV have HIV–HCV co-infection, with the highest burden found in the African and South East Asia regions.[4] People with all three co-infections have high morbidity and mortality compared with those who are negative for all infections or mono-infected.[5 6] Similarly, studies have shown a higher risk of

various comorbidities such as liver cirrhosis, liver cancer and end-stage renal disease among people with co-infection.[7 8]

Despite high morbidity and mortality related with co-infections, limited data are available on co-infections with all three infections at the broader population level.[9] Most studies on co-infection were conducted among people with HIV infection or in specific populations.[4 10–15] Such data are especially scarce in developing countries with high burden of each of these infections, such as Rwanda.[12 16] In 2015, Rwanda DHS showed that the prevalence of HIV in the general population was 3%, with a higher prevalence in urban than rural areas (6% vs 2.4%, respectively).[17] Recent studies on HBV in Rwanda revealed that the prevalence of hepatitis B surface antigen (HBsAg) among people screened was 3.9%,[18 19] while the prevalence of anti-HCV was between 6.2% and 6.6% with viremia of 52%.[20 21] In 2017, a study conducted among PLHIV found that the prevalence of co-infections with HBV and HCV were 4.2% and 4.7%, respectively.[16]

Rwanda is among few African countries that have committed to fight HBV and HCV, in addition to HIV, and to eliminate them before 2030.[22] Scale-up of treatments for HBV, HCV and HIV has the potential to reduce morbidity and mortality. However, for co-infections, treatment decisions and outcomes differ, thus, there is a need to better characterise the burden of co-infections of these diseases in the general population in Rwanda. Quantifying the burden of these co-infections will inform effective screening, diagnosis and treatment programmes.

HBV, HCV and HIV share transmission routes, and their co-occurrence depends on the presence of shared risk factors and community prevalence rates. Furthermore, the presence of multiple risk factors can interact with each other to increase the risk of infection transmission, a concept also known as a syndemic.[23] Some of these risk factors, as well as the infection, may also enhance morbidity and mortality caused by all or one of these three viruses. For instance, in British Columbia, Canada, substance use was associated with a higher risk of triple infection and HCV–HIV co-infection, while men having sex with men had a higher risk of HIV and HIV–HBV co-infection.[9] In a study on HBV, HCV and HIV in Libya, co-infection prevalence was low (HCV/HIV: 0.15%, HCV/HBV: 0.04%, HBV/HIV: 0.03%). HIV, HCV and their co-infection were related to substance use and hemodialysis, while HBV infection was associated with family history and contact with person living with HBV.[9] This pattern is unlike in Sub-Saharan Africa, where HBV is commonly transmitted during childhood between siblings long before infection of HIV and HCV.[11] Risk factors might be different in different countries due to differences in the characteristics of general population; therefore, it is crucial to identify risk factors associated with these co-infections in Rwanda. Characterisation of risk factors and their relationships in high prevalence subpopulations could inform the optimisation of services for various population groups at risk of and affected by HBV, HCV, HIV as well as other blood-borne infections.

Thus, this study aims to address these gaps by assessing the burden of the HBV, HCV HIV and their co-infections and characterising underlying factors among people tested during the 2019 mass screening in six districts of Rwanda.

METHODS

Study design

The study is a secondary analysis of cross-sectional data collected during the 2019 screening campaign for viral hepatitis through the use of a standardised laboratory request form which contained sociodemographic, comorbidities and known viral hepatitis risk factors. HBV DNA and HCV RNA were also assessed.

Setting

The campaign was conducted at 60 health centres across six districts (10 by each district). Three districts were in Kigali which, in 2016, had a high prevalence of HIV infection (6%),[17] HIV/HBsAg co-infection (5.0%) and HIV/anti-HCV co-infection (4%).[16] One district was from Northern Province which, in 2017, was shown to have a high viremia rate of HCV (61.43%) among 9.11% screened anti-HCV positives.[20] Two districts were from Western Province, which in 2016 had prevalence of 3% for both co-infection HIV/HBsAg and HIV/anti-HCV.[16]

Patient and public involvement

This analysis is performed on data collected as part of screening campaign. Patients/public were not involved in the design and interpretation of analyses presented in this paper.

Study population and recruitment of participants

At each of the 10 screening site health centres, individuals 15 years of age and older were invited to participate in viral hepatitis screening. Health centres were selected according to population size so that participants did not need to travel more than 2 km to the closest screening site. People who were not Rwandan by nationality or were under 15 years old were excluded. From April to May 2019, screening campaigns were conducted for 2 weeks in each district. This study included individuals who met the screening criteria of the targeted demographic groups and attended screening sites (health centres) for HCV and HBV testing. Patients who were diagnosed with one or more of these infections were referred to care and treatment services for further management.

Data collection procedures

After obtaining verbal consent, and verbal assent from parents or guardians of children aged 15–18 years, data on demographic, clinical and behaviour characteristics were obtained by trained nurses and laboratory technicians using a laboratory request form. Information regarding exposure to known risk factors of these infections

included history of blood transfusions, surgical interventions, and traditional operations or scarifications. Other comorbidities, such as cardiovascular diseases, diabetes and cancer, were also collected.

Testing methods

Laboratory testing was performed using SD Bioline Rapid tests for anti-HCV with sensitivity of 98.9% and specificity of 99.7%[24] and HBsAg with sensitivity of 90% and specificity of 99.5%.[25] A team of laboratory technicians trained on viral hepatitis testing from the National Reference Laboratory supervised all testing activities. When laboratory results were available, the results and the contents of the laboratory request form were immediately entered in a password-protected database (Microsoft Excel database). Each day, blood samples from individuals testing positive on the HCV and/or HBV screening test collected at health centres were transferred immediately to HCV RNA and HBV DNA testing sites. HCV RNA and HBV DNA testing were performed at seven accredited laboratories serving as hubs of the National Reference. HCV RNA and HBV DNA testing were conducted using COBAS AmpliPrep/COBAS TaqMan HCV and HBV Test, V.2.0: Quantitative (Roche) with a lower limit of quantification of 15 IU/mL. HIV results were self-reported at screening site, but all participants who tested positive for HCV and HBV were retested for HIV using Alere HIV-Combo-Determine (Alere, Waltham) as the screening test and confirmed by HIV ½ STAT-PAK (Medford, NY, USA) if reactive. Results from these testing sites were entered into the database. The database was de-identified for the present study and the study team did not have access to patient identification information.

Variables

The outcomes of interest included chronic HCV infection, chronic HBV infection, HIV infection, co-infection HIV/HBV, co-infection HIV/HCV, co-infection HBV/HCV and co-infection HCV/HBV/HIV.

Data were collected on sociodemographic characteristics including age, sex, urbanicity, socioeconomic status (Ubudehe category) and marital status. Age was categorised into five groups: less than 35 years old, 35–44 years old, 45–54 years old, 55–64 years old and over 65 years old. Urbanicity was defined as living in town or not. Socioeconomic status was categorised based on 'Ubudehe', a mechanism of the Rwanda Ministry of Local Government, whereby citizens are placed into different socioeconomic categories ranging from 1 to 4.[26 27] The lowest socioeconomic category is 1 (poorest) and the highest is 4 (richest). For health insurance, only community-based health insurance (Mutuelle), la Rwandaise Assurance Maladie (RAMA) and Medical Military Insurance (MMI) were categorised separately; all other insurances were categorised as 'private insurances'. The RAMA health insurance is a public-operated health insurance available to individuals currently and formally employed in both public and private sectors. Marital status was categorised into three groups of married, single and widowed, separated or divorced. Self-reported comorbidities assessed included cardiovascular diseases, diabetes, chronic renal failure and cancer.

Assessed risk factors that were associated with parenteral routes of transmission included history of health facility–based surgical operation, traditional surgical operation and transfusion. Traditional surgical operation practices are defined as scarifications, male circumcision, tattoos, traditional dental extraction or uvulectomy done by a community member or traditional practitioner. Other assessed factors included the number of sexual partners and self-reported presence of diagnosed viral hepatitis of a family member. All these exposures to viral hepatitis risk factors were self-reported.

The Medical Research Council of Rwanda controlled the ethical procedures for data collection and the authorisation to conduct these activities in different sites was obtained from the Ministry of Health. The approval for utilisation of these data was obtained by Rwanda Biomedical Center (No. 2048/RBC/2019) as this study concerned data collected during viral hepatitis screening and testing.

Statistical methods and data analysis

Data cleaning and analysis was conducted in SPSS V.20.0. In univariate analysis, we estimated the prevalence of mono-infections and co-infections, and described characteristics of study population. In bivariate analysis, Pearson χ^2 test was used to test for association between categorical or binary variables and the seven outcomes of interest. Potential determinants for each outcome of interest were assessed in bivariable and multivariable models using logistic regressions.

All variables in bivariate analyses were considered for inclusion in multivariable regression model if their inclusion was conceptually logical regardless of statistical significance or if their corresponding p value was <0.1. Variables were kept in the final model if they were significant at 5% level of significance. We reported ORs with their corresponding CIs.

RESULTS

Data regarding participant characteristics and results for all three infections were available for 156 499 of the 164 225 campaign participants (95.3%). Those who were excluded was due to lack of data or not being in the target population.

Sample characteristics

Sociodemographic characteristics of participants included in the analysis are shown in table 1. The median age of participants was 35 years (IQR 18–58), with most participants (24.3%) in the group aged 25–34 years as shown in table 1. Most of the participants (67.1%) were female and 59.0% of participants were married. Half (50.2%) of participants were in Ubudehe category 3, and nearly all

Table 1 Descriptive characteristics of sociodemographic for participants tested

Characteristics	Frequency (n (%))	Negatives (n (%))	HBV (n (%))	HBV HIV (n (%))	HBV HCV (n (%))	HCV (n (%))	HBV HCV HIV (n (%))	HCV HIV (n (%))	HIV (n (%))
Row (%)	156 449 (100)	146 103 (93.4)	3465 (2.2)	158 (0.1)	38 (0.02)	3163 (2.0)	3 (0.002)	238 (0.15)	4154 (2.7)
Gender (n=156 499)									
Female	104 953 (67.1)	98 057 (93.4)	1918 (1.8)	103 (0.1)	21 (0.02)	2143 (2.1)	1 (0.001)	163 (0.2)	3122 (3.0)
Male	51 496 (32.9)	48 046 (93.3)	1547 (3.0)	55 (0.1)	17 (0.003)	1020 (2.0)	2 (0.004)	75 (0.1)	1032 (2.0)
Age group in years (n=154 489)									
15–24	35 882 (23.2)	35 534 (99.0)	40 (1.1)	8 (0.02)	2 (0.01)	87 (0.2)	0 (0)	10 (0.04)	241 (0.7)
25–34	37 593 (24.3)	35 776 (95.2)	1004 (2.7)	18 (0.05)	7 (0.02)	206 (0.6)	0 (0)	32 (0.1)	664 (1.8)
35–44	33 670 (21.8)	31 270 (92.9)	1025 (3.0)	59 (0.2)	9 (0.03)	317 (1.0)	2 (0.06)	47 (0.3)	1175 (3.5)
45–54	20 606 (13.3)	18 805 (91.3)	498 (2.4)	49 (0.2)	9 (0.04)	355 (1.7)	1 (0.05)	52 (0.2)	1059 (5.2)
55–64	17 112 (11.1)	15 462 (90.4)	304 (1.8)	18 (0.1)	4 (0.02)	716 (4.2)	0 (0)	38 (0.3)	690 (4.1)
65 and above	9626 (6.2)	7965 (82.7)	131 (1.4)	4 (0.04)	6 (0.06)	1343 (14.0)	0 (0)	56 (0.6)	253 (2.7)
Marital status (n=155 295)									
Single	47 565 (30.6)	45 711 (96.1)	852 (1.8)	32 (0.1)	8 (0.02)	255 (0.5)	1 (0.002)	31 (0.1)	818 (1.7)
Married	91 547 (59.0)	85 554 (93.5)	2286 (2.5)	86 (0.1)	19 (0.02)	1800 (2.0)	2 (0.002)	137 (0.1)	2149 (2.4)
Widowed, divorced and separated	16 183 (10.4)	13 834 (85.5)	296 (1.8)	40 (0.2)	11 (0.07)	980 (6.1)	0 (0)	40 (0.4)	1164 (7.3)
Ubudehe category (n=154 703)									
Category 1	17 105 (11.1)	15 609 (91.3)	312 (1.8)	32 (0.2)	6 (0.04)	492 (2.9)	0 (0)	35 (0.2)	765 (4.5)
Category 2	59 634 (38.5)	55 723 (93.4)	1245 (2.1)	60 (0.1)	15 (0.03)	1118 (1.9)	1 (0.003)	81 (0.1)	1704 (2.9)
Category 3	77 722 (50.2)	73 227 (94.2)	1691 (2.2)	63 (0.1)	17 (0.02	1376 (1.8)	2 (0.002)	118 (0.2)	1626 (2.1)
Category 4	242 (0.2)	230 (95.0)	8 (3.3)	0 (0)	0 (0.00)	2 (0.8)	0 (0)	0 (0)	2 (0.8)
Health insurance (n=155 811)									
Mutuelle	146 443 (94.0)	136 755 (93.4)	3145 (2.1)	144 (0.1)	36 (0.02)	3020 (2.1)	3 (0.002)	217 (0.1)	3920 (2.7)
RAMA	6957 (4.5)	6604 (94.9)	185 (2.7)	2 (0.03)	2 (0.03)	61 (0.9)	0 (0)	12 (0.2)	123 (1.8)
MMI	1202 (0.8)	1140 (94.8)	44 (3.7)	0 (0)	0 (0)	8 (0.7)	0 (0)	2 (0.2)	12 (1.0)
Other private insurances	1209 (0.8)	1038 (85.9)	75 (6.2)	9 (0.7)	0 (0)	56 (4.7)	0 (0)	6 (0.5)	55 (4.6)
Urbanicity (n=156 449)									
Yes	76 664 (47.1)	69 683 (90.9)	2068 (2.8)	106 (0.1)	15 (0.04)	1334 (1.8)	3 (0.004)	109 (0.1)	3809 (3.8)
No	82 785 (52.9)	78 396 (94.7)	1408 (1.7)	52 (0.1)	12 (0.01)	1829 (2.2)	0 (0)	129 (0.1)	1345 (1.7)

HBV, hepatitis B virus; HCV, hepatitis C virus; MMI, Medical Military Insurance; RAMA, la Rwandaise Assurance Maladie.

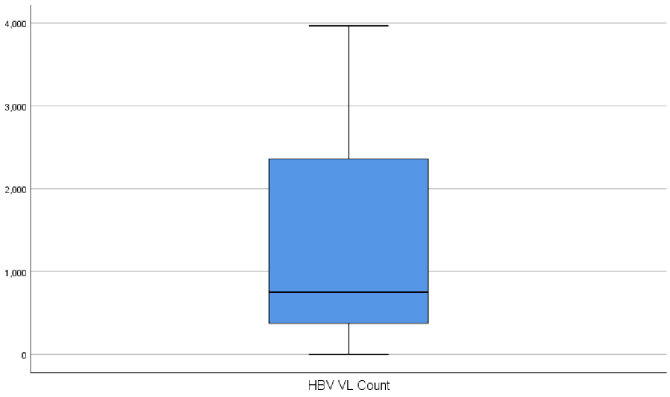

Figure 1 Distribution of quantity of hepatitis B virus (HBV) DNA copies by population. VL, viral load.

(94.0%) participants were enrolled in the community-based health insurance (Mutuelle). Over half (52.7%) were from rural districts. Among all participants, 4.4% had a history of operation at least once, and 10.2% had a history of traditional surgical and scarification practice while 5.2% of participants experienced physical trauma assault at least once.

Infection prevalence

Overall, 3465 (2.2%) were HBsAg positive and of those, 2872 (82.9%) had HBV DNA detectable with median of 751 copies/mL (IQR 400–2500) of HBV DNA (figure 1). In addition, 4382 (2.8%) were anti-HCV positive and among them 3163 (72.2%) had HCV RNA detectable with a median of 567 000 copies/mL (IQR 300 000–580 000) of HCV RNA (figure 2). Overall, 4154 (2.7%) people reported being HIV positive. The highest prevalence of HBV infection (3.0%) was found in the group aged 35–44 years, the highest prevalence for HIV (5.2%) was found in the group aged 45–54 years and for HCV infection it was found in 65 years old and above (14.0%) (table 1). The highest prevalence of HIV was found in people who had more than one lifetime sexual partner, people who had experience of surgery and people who had been transfused with 8.1%, 6.9% and 6.5%, respectively. The highest prevalence of HBV was found in people who had a family relative or ever been diagnosed and in people who had experience of surgery with 4.9%, 3.6% and 3.3%, respectively. Finally, HCV was more common in people who had a family relative with HCV history and in people who had experience of traditional operation or scarification with 3.6% and 3.5%, respectively (table 2).

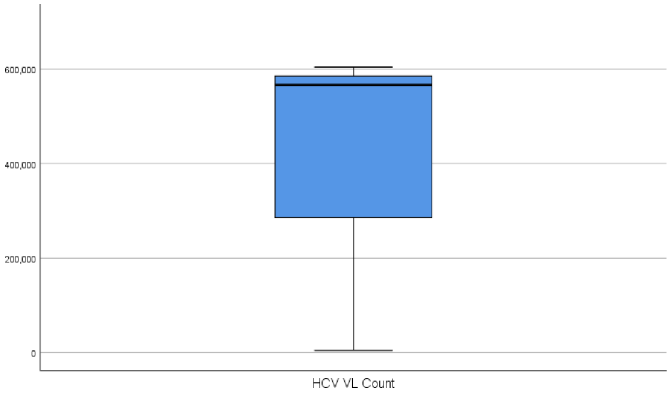

Figure 2 Distribution of quantity of hepatitis C virus (HCV) RNA copies by population. VL, viral load.

Characteristics of people with co-infection

HIV/HBV co-infection was found in 158 participants (0.1%), HIV/HCV in 238 participants (0.15%) and HCV/HBV in 38 participants (0.02%). The triple infection HIV/HCV/HBV was found in three individuals (0.002%) of all participants. The highest prevalence for HBV/HCV/HIV co-infection (0.06%) and HBV/HIV co-infection (0.2%) were among people aged 35–44 years. The highest prevalence for HCV/HBV co-infection (0.07%), HCV/HIV co-infection (0.4%) and HBV/HIV co-infection (0.2%) was found in group of widows, divorced and separated. More details are shown in table 1.

Factors associated with various infections

Significant associations with HBV infection were being male (OR 1.77, 95% CI 1.64 to 1.90), living in town (OR 1.57, 95% CI 1.46 to 1.69), ever been diagnosed with liver disease (OR 1.92, 95% CI 1.53 to 2.40), history of surgical operation (OR 1.50, 95% CI 1.30 to 1.74), exposure to traditional operational practices and scarification (OR 1.57, 95% CI 1.41 to 1.74), and having a person in the family with viral hepatitis (OR 1.48, 95% CI 1.27 to 1.73).

Significant association with HCV infection were being male (OR 1.17, 95% CI 1.07 to 1.27); being divorced, separated and widowed (OR 1.29, 95% CI 1.06 to 1.57); using other private insurance company (OR 3.15, 95% CI 2.26 to 4.39); ever been diagnosed with liver disease (OR 1.78, 95% CI 1.36 to 2.34); history of surgical operation (OR 1.39, 95% CI 1.19 to 1.63); and exposure to traditional operational practices and scarification (OR 1.44, 95% CI 1.29 to 1.60).

Significant associations with HIV infection were being female (OR 1.18, 95% CI 1.09 to 1.27); living in town (OR 2.23, 95% CI 1.88 to 2.17); being in group of divorced, separated and widowed (OR 2.37, 95% CI 1.98 to 2.83), using other private insurance company (OR 3.08, 95% CI 2.25 to 4.21); ever been diagnosed with liver disease (OR 1.82, 95% CI 1.39 to 2.38); history of surgical operation (OR 1.42, 95% CI 1.21 to 1.66); history of physical traumatic assault (OR 1.69, 95% CI 1.51 to 1.88); and exposure to traditional operational practices and scarification (OR 1.48, 95% CI 1.33 to 1.65).

HBV/HIV co-infections were significantly associated with living in town (OR 2.15, 95% CI 1.50 to 3.07), using other private insurance company (OR 6.41, 95% CI 3.10 to 13.24), ever been diagnosed with liver disease (OR 3.68, 95% CI 1.89 to 7.15), history of surgical operation (OR 2.06, 95% CI 1.25 to 3.40), exposure to traditional operational practices and scarification (OR 2.02, 95% CI 1.28 to 3.18), having more than one lifetime sexual partner (OR 2.02, 95% CI 1.28 to 3.18) and history of physical trauma assault (OR 1.82, 95% CI 1.08 to 3.05).

Table 2 Descriptive characteristics of risk factors and comorbidities for participants tested

Characteristics	Frequency (n (%))	Negatives (n (%))	HBV (n (%))	HBV HIV (n (%))	HBV HCV (n (%))	HCV (n (%))	HBV HCV HIV (n (%))	HCV HIV (n (%))	HIV (n (%))
History of diabetes (n=156 449)									
No	150 104 (95.9)	143 519 (95.6)	3380 (2.3)	154 (0.1)	36 (0.02)	2956 (2.0)	3 (0.002)	220 (0.1)	4042 (2.7)
Yes	1598 (1.0)	1497 (93.7)	30 (1.9)	2 (0.1)	0 (0)	51 (3.2)	0 (0)	7 (0.4)	59 (3.7)
Don't know	4747 (3.1)	4553 (95.9)	55 (1.2)	2 (0.04)	2 (0.02)	156 (3.3)	0 (0)	11 (0.2)	53 (1.7)
History of cardiovascular diseases (n=156 449)									
No	147 799 (94.0)	141 862 (95.6)	3322 (2.2)	146 (0.1)	34 (0.02)	2762 (1.9)	3 (0.002)	220 (0.1)	3927 (2.7)
Yes	3906 (2.5)	390 (88.6)	88 (2.3)	10 (0.2)	2 (0.05)	244 (6.3)	0 (0)	7 (0.2)	175 (4.5)
Don't know	4744 (3.0)	7317 (95.5)	55 (1.2)	2 (0.04)	2 (0.04)	157 (3.3)	0 (0)	11 (0.2)	52 (1.7)
History of CRF (n=156 448)									
No	150 296 (96.1)	143 713 (95.6)	3378 (2.2)	153 (0.1)	35 (0.02)	2965 (2.0)	3 (0.002)	220 (0.1)	4029 (2.7)
Yes	934 (0.6)	849 (90.9)	22 (2.4)	3 (0.3)	1 (0.1)	18 (1.9)	0 (0)	2 (0.5)	73 (7.8)
Don't know	5218 (3.3)	5006 (95.9)	64 (1.2)	2 (0.04)	2 (0.04)	180 (3.5)	0 (0)	16 (0.2)	52 (1.7)
History of cancer (n=156 449)									
No	148 351 (94.8)	141 862 (95.6)	377 (2.1)	156 (0.1)	34 (0.02)	2958 (2.0)	3 (0.002)	220 (0.1)	3944 (2.7)
Yes	440 (0.3)	390 (88.6)	12 (2.7)	0 (0)	2((0.5)	18 (4.2)	0 (0)	2 (0.2)	36 (8.2)
Don't know	7658 (4.9)	7317 (95.5)	76 (1.0)	2 (0.03)	2 (0.03)	187 (2.5)	0 (0)	16 (0.3)	174 (3.1)
Ever been diagnosed with hepatitis (n=156 437)									
No	154 648 (98.8)	147 886 (95.6)	3377 (2.2)	148 (0.1)	38 (0.02)	3099 (2.0)	3 (0.002)	220 (0.1)	4072 (2.7)
Yes	1789 (1.1)	1670 (93.3)	88 (4.9)	10 (0.6)	0 (0)	64 (3.6)	0 (0)	16 (1.2)	81 (4.5)
Ever been operated on (n=156 438)									
No	149 509 (95.6)	143 240 (95.8)	3238 (2.2)	138 (0.1)	34 (0.02)	2949 (2.0)	3 (0.002)	211 (0.1)	3706 (2.5)
Yes	6929 (4.4)	6119 (88.3)	229 (3.3)	20 (0.3)	4 (0.06)	214 (3.1)	0 (0)	27 (0.4)	647 (6.5)
Ever been transfused (n=156 439)									
No	152 420 (97.4)	145 884 (95.7)	3388 (2.2)	150 (0.1)	38 (0.02)	3088 (2.0)	3 (0.002)	237 (0.1)	3876 (2.2)
Yes	4019 (2.6)	3682 (91.6)	77 (1.9)	8 (0.2)	0 (0.0)	75 (1.9)	0 (0)	7 (0.1)	277 (6.9)
Viral hepatitis in the family (n=156 409)									
No	147 287 (94.1)	140 901 (95.7)	3223 (2.2)	147 (0.1)	34 (0.02)	2896 (2.0)	3 (0.002)	205 (0.1)	3879 (2.7)
Yes	5431 (3.5)	5103 (94.0)	197 (3.6)	10 (0.2)	2 (0.04)	122 (2.3)	0 (0)	18 (0.3)	236 (4.3)
Don't know	3691 (2.4)	3519 (95.3)	5 (0.1)	0 (0)	2 (0.05)	145 (3.9)	0 (0)	9 (0.2)	38 (1.2)
Traditional operation and scarification (n=156 424)									
No	140 402 (89.8)	134 824 (96.0)	2959 (2.1)	119 (0.1)	29 (0.02)	2618 (1.9)	2 (0.001)	193 (0.1)	3303 (2.4)

Continued

Table 2 Continued

Characteristics	Frequency (n (%))	Negatives (n (%))	HBV (n (%))	HBV HIV (n (%))	HBV HCV (n (%))	HCV (n (%))	HBV HCV HIV (n (%))	HCV HIV (n (%))	HIV (n (%))
Yes	16 022 (10.2)	14 723 (91.9)	506 (3.2)	39 (0.2)	9 (0.06)	545 (3.5)	1 (0.006)	45 (0.3)	848 (5.4)
Having more than one lifetime sexual partner (n=156 437)									
No	148 077 (94.7)	141 991 (95.9)	3248 (2.2)	133 (0.)	34 (0.02)	2993 (2.0)	2 (0.001)	214 (0.1)	3476 (2.4)
Yes	8360 (5.3)	7567 (90.5)	217 (2.6)	25 (0.3)	4 (0.05)	170 (2.2)	1 (0.01)	24 (0.3)	677 (8.1)
Ever experienced of physical trauma assault (n=156 437)									
No	148 300 (94.8)	142 020 (95.8)	3260 (2.2)	139 (0.1)	34 (0.02)	2962 (2.0)	2 (0.001)	225 (0.2)	3718 (2.5)
Yes	8137 (5.2)	7538 (92.6)	205 (2.5)	19 (0.2)	4 (0.05)	201 (2.5)	1 (0.01)	13 (0.2)	435 (5.3)
HBV vaccination (n=156 449)									
Not vaccinated	144 322 (92.2)	138 197 (95.8)	3175 (2.2)	131 (0.1)	35 (0.03)	2931 (2.0)	2 (0.001)	128 (0.1)	3490 (2.4)
Fully vaccinated	10 323 (6.6)	9684 (93.8)	217 (2.1)	24 (0.2)	3 (0.02)	200 (2.0)	1 (0.01)	107(1)	574 (5.7)
Partially vaccinated	1804 (1.2)	1688 (93.6)	73 (4.0)	3 (0.2)	0 (0.0)	32 (1.8)	0 (0)	3 (0.2)	90 (5.0)

CRF, chronic renal failure; HBV, hepatitis B virus; HCV, hepatitis C virus.

HIV/HCV co-infection was associated with using other private insurance company (OR 3.24, 95% CI 1.32 to 7.94), ever been diagnosed with liver disease (OR 6.67, 95% CI 4.17 to 10.67), history of surgical operation (OR 2.01, 95% CI 1.32 to 3.07), and exposure to traditional operational practices and scarification (OR 1.50, 95% CI 1.07 to 2.12).

However, lower odds were found for HBV and HCV infection in people who were transfused (OR 0.69, 95% CI 0.54 to 0.87 and OR 0.73, 95% CI 0.57 to 0.94**,** respectively). We also found lower odds for HIV/HBV co-infection and HIV infection in Ubudehe category 2 compared with category 1. Having civil servant health insurances and being in Ubudehe categories 3 and 4 (RAMA and MMI) were associated with a reduced odds of HIV infection. Lastly, people living in town were less likely to have HBV/HCV co-infection. More details on risk factors associated with all these co-infections are illustrated in table 3.

DISCUSSION

In this large population-based study in Rwanda, we characterised HBV, HCV and HIV co-infections. Overall, mono-infection with any of these viruses was more common and only 0.3% of people tested had double or triple co-infections with HIV/HBV, HIV/HCV or HIV/HBV/HCV. In addition to differences in the patterns of infections, we also found different patterns of risk factors for the different mono-infections and co-infections. For instance, having more than one lifetime sexual partner, being wounded by physical assault, healthcare exposures and urbanicity were associated with higher odds of HIV and HBV/HIV co-infection. On the other hand, rural residence and being in higher wealth category (Ubudehe categories 2, 3, 4) were associated with lower odds of HIV and HBV/HIV co-infection. Scarification, operation from traditional healers and surgical operations were associated with HCV. Lastly, HBV mono-infection risk was associated with family history of infection, urbanicity, operation from traditional healers and surgical operations. These data highlight that although there are some overlaps in risk factors, there are distinct patterns of transmission of these infections indicated by relatively low co-infection levels.

In this study, we found low levels of the different co-infections of the three viruses. This is different from findings from other high-income or low-income and middle-income countries that showed higher rates of these co-infections. For instance, a study conducted in China among people with HIV found that 8.7% of participants had HBV/HIV co-infection, 18.2% had HCV/HIV co-infection and 3.3% triple infection.[5] Another study in British Columbia found co-infection rates higher than those estimated in this study with HCV/HBV at 4.0%; HBV/HIV, 0.7%; HCV/HIV, 3.4%; and co-infection HBV/HCV/HIV at 1.2%.[9] In contrast, a previous study conducted in Rwanda found very low prevalence of HBV/HCV/HIV among PLHIV (0.002%).[16] In addition

Table 3 ORs derived from a multivariable multivariate logistic regression model characterising the association of demographic, risk factor and comorbidity variables with HBV, HCV infection groups and their confections with HIV

Characteristics	HBV (OR (95% CI))	HBV HIV (OR (95% CI))	HCV (OR (95% CI))	HCV HIV (OR (95% CI))	HIV (OR (95% CI))
Gender					
Female	1	–	1	–	**1.18 (1.09 to 1.27)**
Male	**1.77 (1.64 to 1.90)**	–	**1.17 (1.07 to 1.27)**	–	1
Age group in years					
Less than 45	1	**1**	**1**	**1**	**1**
45–64	**0.81 (0.74 to 0.88)**	**1.67 (1.15 to 2.42)**	**3.90 (3.48 to 4.37)**	**2.25 (1.61 to 3.15)**	**1.83 (1.69 to 1.97)**
65 and above	**0.49 (0.40 to 0.60)**	**0.35 (0.12 to 0.98)**	**19.84 (17.64 to 22.30)**	**5.11 (3.45 to 7.59)**	**0.86 (0.74 to 0.99)**
Marital status					
Single	1	1	1	1	1
Married	**1.40 (1.28 to 1.52)**	1.04 (0.67 to 1.61)	**1.70 (1.44 to 1.98)**	1.48 (0.95 to 2.32)	1.08 (0.99 to 1.19)
Widowed, separated and divorced	**1.40 (1.20 to 1.63)**	**2.16 (1.26 to 3.73)**	**2.37 (1.98 to 2.83)**	**2.62 (1.55 to 4.42)**	**2.50 (2.23 to 2.80)**
Ubudehe category					
Category 1	1	1	1	1	1
Category 2	1.04 (0.91 to 1.18)	**0.58 (0.37 to 0.91)**	0.97 (0.86 to 1.09)	0.88 (0.58 to 1.34)	**0.71 (0.65 to 0.78)**
Categories 3 and 4	1.08 (0.95 to 1.23)	**0.54 (0.34 to 0.85)**	0.98 (0.87 to 1.10)	1.05 (0.85 to 1.06)	**0.59 (0.53 to 0.65)**
Health insurance					
Community-based health insurance	1	1	1	1	1
RAMA	**1.18 (1.01 to 1.38)**	0.38 (0.09 to 1.53)	0.60 (0.45 to 0.79)	1.32 (0.71 to 2.46)	0.84 (0.70 to 1.02)
MMI	**1.55 (1.14 to 2.11)**	–*	0.74 (0.35 to 1.56)	1.86 (0.46 to 7.57)	**0.52 (0.30 to 0.93)**
Other private insurances	**2.81 (2.19 to 3.61)**	**6.41 (3.10 to 13.24)**	3.08 (2.25 to 4.21)	**3.24 (1.32 to 7.94)**	**1.46 (1.09 to 1.96)**
Urbanicity					
No	1	1	1	–	1
Yes	**1.57 (1.46 to 1.69)**	**2.15 (1.50 to 3.07)**	**0.88 (0.82 to 0.96)**	–	**2.23 (2.08 to 2.39)**
Ever been diagnosed with hepatitis					
No	1	1	1	1	1
Yes	**1.92 (1.53 to 2.40)**	**3.68 (1.89 to 7.15)**	**6.67 (4.17 to 10.67)**	0.99 (0.78 to 1.26)	
Ever been operated on					
No	1	1	1	1	1
Yes	**1.50 (1.30 to 1.74)**	**2.06 (1.25 to 3.40)**	**1.42 (1.21 to 1.66)**	**2.01 (1.32 to 3.07)**	**1.94 (1.74 to 2.18)**
Ever been transfused					
No	1	–	1	–	1

Continued

Table 3 Continued

Characteristics	HBV (OR (95% CI))	HBV HIV (OR (95% CI))	HCV (OR (95% CI))	HCV HIV (OR (95% CI))	HIV (OR (95% CI))
Yes	**0.68 (0.54 to 0.87)**	–	**0.74 (0.57 to 0.94)**	–	**1.48 (1.29 to 1.70)**
Viral hepatitis in the family					
No	1	1	1	1	1
Yes	**1.48 (1.27 to 1.73)**	1.01 (0.52 to 1.97)	0.93 (0.76 to 1.13)	1.43 (0.91 to 2.25)	0.98 (0.85 to 1.13)
Traditional operation and scarification					
No	1	1	1	1	1
Yes	**1.57 (1.41 to 1.74)**	**2.02 (1.28 to 3.18)**	**1.48 (1.33 to 1.65)**	**1.50 (1.07 to 2.12)**	
Having more than one lifetime sexual partner					
No	1	1	1	1	1
Yes	1.0 (0.87 to 116)	**2.02 (1.28 to 3.18)**	0.93 (0.79 to 1.10)	1.43 (0.91 to 2.25)	
Ever experienced traumatic physical assault					
No	1	1	1	–	1
Yes	1.05 (0.90 to 1.22)	**1.82 (1.08 to 3.05)**	1.11 (0.95 to 1.30)	–	**1.69 (1.51 to 1.88)**

Highlighted results are significant.
*Both bivariable and multivariable regression analyses were conducted, but in this table, only multivariable analysis was presented.
.HBV, hepatitis B virus; HCV, hepatitis C virus; MMI, Medical Military Insurance; RAMA, la Rwandaise Assurance Maladie.

to Rwanda, our findings are also similar to findings of a study conducted in Libya that found low co-infections of HCV/HIV, HCV/HBV, HBV/HIV and HBV/HCV/HIV at 0.15%, 0.04%, 0.03% and 0.02%, respectively.[11] This may relate to differences in patterns of risk factors in various population groups in which specific infections have high prevalence or differences in testing patterns of people with different risk profiles. It may also be due to who shows up for testing at the clinics (self-selection).

Increased odds of HIV and HBV/HIV co-infections were associated with having more than one lifetime sexual partner, while decreased odds were associated with belonging to higher wealth category. Furthermore, living in urban area was also associated with HIV, HBV and HBV/HIV. These findings highlight that individuals with low socioeconomic status, those who live in urban areas and those having more than one lifetime sexual partner are at higher risk of HIV, HBV and their co-infections. Findings from another study conducted among HIV pregnant women in Rwanda showed that women from urban areas were more affected by HIV/HBV co-infection than those from rural areas.[28] HIV shares the same mode of transmission as HBV infection, but the fact that they also share contextual risk factors including urbanicity and low socioeconomic status provides valuable information for their prevention, screening and treatment efforts in Rwanda. It means that strategies that work for one may be effective for both.

Male sex was associated with higher risk of HCV and HBV. This may be due to greater mobility or involvement in armed conflict in this region of Africa. For HCV, this finding might be due to a greater number of traditional healing/surgeries and tattoos practised more by males than females. Higher odds for HBV were associated with higher frequencies of sexual encounters and, perhaps, more exposure to casual sex workers through mobile employment. These findings are similar to other studies done in Rwanda[18 21 29] and in Burkina Faso.[30] Contrary to HIV and HBV, HCV infection was more common in rural areas, and this is consistent with previous findings from Rwanda and other African countries.[16 20 30] A study conducted in Kenya among people who inject drugs found higher prevalence of HCV and HCV/HIV co-infection in Coastal Kenya compared with Nairobi.[31] The higher burden of unsafe medical practices by licensed practitioners and traditional healers could explain the higher prevalence of HCV in rural areas. Unsafe medical practices are known to be associated with HBV, HCV and HIV infections in different settings globally.[32 33] The association of scarification and unsafe medical practices by traditional healers with higher odds of HBV and HCV has been previously described in Rwanda.[21 29] Unfortunately, these unsafe practices are still highly prevalent in Rwanda. One notable example is male circumcision performed outside of a healthcare facility. The recent Demographic and Health Survey (DHS 2015) found that 10% of men across all age groups had been circumcised through unsafe practices.[17] Taken together, these data show that there is an urgent need for improvement in infection control practices in the non-community setting.[34] Although highly effective curative and suppressive therapy could treat infections and reduce the prevalence and new infections, optimising prevention of these infections is essential to achieve hepatitis elimination goal.

This study has several limitations. First, the demographic profile of the sample population of voluntary participants differed from the Rwandan population at large, with a substantially greater proportion of women (67.1%) than the general population. Moreover, participants were from six districts only. Therefore, the prevalence estimates and risk factors found to be associated with HCV, HBV, HIV and their co-infections may not be generalisable to the entire Rwandan population and may have been underestimated. The study did not include data on certain known risk factors such as exposure to wars and other conflict resulting in sexual violence or refugee status, occupational risk and injection drug use. However, unlike high-income countries, the number of individuals who inject drugs are low in Rwanda.[35]

Lastly, this study relied on routinely collected and self-report data to assess clinical variables (eg, history of diabetes) or historical exposure which may have led to misclassification due to imperfect recall. However, since infection status was not known at the time of interview, it is likely that recall is non-differential.

CONCLUSIONS

To conclude, prevalence of HBV, HCV and HIV infections in Rwanda are higher than many other countries. Overall, the majority of people with an infection had single infection with one of these viruses, with less than 0.3% having co-infections of HIV/HBV or HIV/HCV or HIV/HBV/HCV. Patterns of risk factors for mono-infection and co-infections differ. HIV and related co-infections are associated with high risk of sexual behaviours, urbanicity and healthcare risk factors, while HCV and related co-infections mostly are associated with rurality and unsafe medical practices. The findings from this study identify areas for strengthening prevention of bloodborne infections in Rwanda which is critical to achieving WHO elimination goals. These findings will also be informative for other countries in Sub-Saharan Africa that may have a context similar to Rwanda.

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