HCV Seroprevalence among HIV Patients and Associated Comorbidities at One Primary Health Facility in Rwanda

Jean Bosco Munyemana,^{1*} Esperance Mukanoheli,² Theoneste Nsabimana,^{3*} and Jean Damascene Niringiyumukiza⁴

¹Department of Clinical Biology, School of Medicine and Pharmacy, College of Medicine and Health Sciences, University of Rwanda, Kigali, Rwanda; ²Department of Biomedical Laboratory Sciences, Faculty of Applied Fundamental Sciences, INES-Ruhengeri, Musanze, Rwanda;

³Department of Internal Medicine, Kibagabaga District Hospital, Kigali, Rwanda; ⁴Department of Obstetrics and Gynecology, Reproductive Endocrinology and Infertility Clinic, Rwanda Military Hospital, Kigali, Rwanda

Abstract. Hepatitis C virus (HCV) and HIV have emerged as major viral infections within the past two decades, and their coinfection poses a big challenge with a significant impact in terms of morbidity and mortality associated with liver disease and renal failure. The current study aimed at assessing the prevalence of HCV infection and associated comorbidities among HIV patients at one primary health facility in Rwanda. In total, 417 HIV-positive patients were recruited and included in the study from January 1, 2019 up to June 30, 2019. All participants were screened for HCV infection by using the SD Bioline HCV antibody rapid test. In addition, underlying medical conditions were also recorded as comorbidities. Among 417 participants, 52 exhibited HCV-positive results (12.5%). The group of 41- to 50- and 51- to 60-year-olds had higher prevalence of HIV/HCV coinfection than other age-groups with 3.6% and 4.6%, respectively. Furthermore, five underlying medical conditions were found as comorbidities among the study participants. Those with HIV/HCV coinfection showed higher comorbidities than those with mono-infection including liver toxicity, *P* value 0.005; tuberculosis, *P* value 0.005; renal failure, *P* value 0.003; hypertension, *P* value 0.001; and diabetes mellitus, *P* value 0.001. The relative risk ratio of having comorbidities in those groups was 4.09. To conclude, the prevalence of HCV/HIV coinfection is high, and there was a statistical significant association of having comorbidities in HIV/HCV-coinfected group compared with the group of HIV mono-infection, which suggests more intervention in this vulnerable group of patients.

INTRODUCTION

Hepatitis C virus (HCV) infection is a major cause of liver cirrhosis and hepatocellular carcinoma worldwide.¹ Hepatitis C virus infections are common worldwide, with 3–4 million new infections yearly and infection rates as high as 5% in some countries.² It is estimated that 170 million people 3% of the world's population, have HCV. This estimate is more than four times the number of people living with HIV (PLWH). Moreover, HCV infection is the most associated with HIV infection.³

HIV, which causes AIDS, and HCV are among the major challenges to public health in the world. Both are RNA viruses and share common transmission routes; parenteral, sexual, and vertical. This epidemiological similarity results in a high prevalence of HIV/HCV coinfection and represents an important factor of morbidity and mortality for the affected individuals.⁴ Hepatitis C virus/HIV coinfection is associated with increased HCV viral load in serum/plasma, and this observation has been well described.⁴ Higher HCV viral loads were reported to be associated with a delayed HCV clearance after HCV treatment. Furthermore, longitudinal treatment studies demonstrate that a paradoxical increase in HCV viral load after initiation of combination antiretroviral therapy (cART) for HIV occurs in some patients.⁵ This appears to be more frequent among those with low CD4⁺ T-cell counts at initiation of cART.⁶ Despite the global threat caused by HIV/HCV coinfection with decreased survival, which suggests continued HCV screening in PLWH, the HCV screening-related cost is a big challenge in sub-Saharan countries.

Considering the high cost of HCV screening, routine HCV testing is not always performed among all HIV patients in health settings with limited resources.⁷ However, the overlapping modes of transmission of both HIV and HCV make this coinfection a global public health concern. The recent meta-analysis study has shown that there are 37 million people infected with HIV and 115 million people with antibodies to HCV. In that study, they estimated a global HIV/HCV coinfection prevalence of 2–4%.⁸ Thirty-nine studies from 10 countries in the Asia-Pacific region comprising 89,452 HIV-positive individuals showed that HCV coinfection prevalence was 3.8%.¹ Another previous study has revealed an HIV/HCV coinfection rate of 1.5%, in Abidjan, Cote d'Ivoire, and 6.7% in Cameroon.⁹ Much higher HIV/HCV coinfection rates of 30% and 64.3% were reported in a drug cohort of American and Spanish women, respectively.¹⁰ Furthermore, 59% and 45% were reported in Finland and France.¹¹ Moreover, the reported prevalence varies significantly depending on the geographic region and mode of transmission ranging from 7% by sexual transmission to 91% for injection drug users.¹² In addition to that, higher prevalence of HIV/HCV coinfection was reported to be associated with decreased survival time and life span, increased complications, and emergence of comorbidities.

The emergence of comorbidities with an increased rate of progression to cirrhosis, decompensated liver disease, hepatocellular carcinoma, and death was highlighted and remains critical challenge.^{13,14} Although different studies have been conducted to characterize the prevalence of HCV/HIV coinfection and comorbidities, there are paucity of data regarding characterization of the prevalence of HCV/HIV and associated complications or comorbidities in Rwanda. The current study aimed to determine the prevalence of HCV infection and associated comorbidities among HIV patients at one primary health facility in Rwanda.

* Address correspondence to Jean Bosco Munyemana, Department of Clinical Biology, School of Medicine and Pharmacy, College of Medicine and Health Sciences, University of Rwanda, KK 737 St., P.O. Box 3286, Kigali, Rwanda, E-mail: munyebos1@gmail.com or Theoneste Nsabimana, Department of Internal Medicine, Kibagabaga District Hospital, KG 19 Ave., PO Box 6260, Kigali, Rwanda, E-mail: nsabitheo@gmail.com.

TABLE 1

Demographic characteristics of people living with HIV/AIDS seen at one primary healthcare facility in Rwanda

	Variable	Frequency (%)	P-value
Gender	Male	172 (41.3)	0.7
	Female	245 (58.7)	
Age-group (years)	≤ 20	10 (2.4)	0.0003
	21–30	64 (15.4)	
	31–40	115 (27.6)	
	41–50	110 (26.4)	
	51–60	90 (21.6)	
	≥ 61	28 (6.7)	
Total		417 (100)	

Data are presented as frequency (%) unless otherwise indicated. *P* value less than 0.05 was considered statistically significant (*n* = 417).

MATERIALS AND METHOD

The current study was conducted at Remera Health Centre (RHC), in an antiretroviral treatment (ART) clinic, located in Gasabo district of Kigali city, Rwanda. This study was a cross-sectional study and has recruited 417 PLWH. All participants were screened for HCV infection from January 1, 2019 up to June 30, 2019. All age-groups were included in the study.

Data collection. All recruited participants were HIV positive and were recruited during their regular visit at the RHC in the ART clinic for routine HIV monitoring. After explanation of the nature of the study, the participants who voluntarily accepted to participate in the study were recruited. Demographic characteristics were recorded on a data collection form; existing or underlying comorbidities were also recorded on a data collection form. Blood samples were collected by a trained and experienced laboratory technician at the RHC. The samples were tested using HCV Ab rapid tests according to the manufacturers' instructions.

HCV screening procedure. The SD BIOLINE HCV rapid test (Standard Diagnostics, Inc., Korea) rapid test was used for HCV testing as per the manufacturers' instructions. In brief, venous whole blood was drawn in a 4-mL ethylenediaminetetraacetic acid BD Vacutainer tube (Becton-Dickinson, Franklin Lakes, NJ) and 10 µL of serum/plasma was transferred to the testing device (HCV rapid test). After 20 minutes, test results were read. The samples were recorded as either "positive" if the reactive line and control line were apparent or "negative" if only the control line was apparent. The test sensitivity of the test was ≥ 99.8 (95% CI: 99.0–100), and specificity was 99.9 (95% CI: 99.8–100).

Statistical analysis. Data were recorded in Microsoft Excel sheet (Microsoft Corporation, Redmond, WA) and were exported to SPSS version 22 (IBM SPSS, Turkey) for data analysis. Descriptive statistics were performed to calculate the frequency and percentages of demographic characteristics, HIV mono-infection, HCV/HIV coinfection, and comorbidities among the study participants. Chi-square analysis was performed to test for the associations between HCV/HIV coinfection and having comorbidities. The relative risk (RR) ratio was calculated to determine the risk of having comorbidities in HCV/HIV-coinfected patients. The *P*-value less than 0.05 was considered statistically significant.

Ethical consideration. The ethical clearance number 60/ INES/2018 was obtained from the INES Ruhengeri Institutional Review Board (IRB), and approval to conduct the study was obtained from the RHC. In addition, the participants

who have accepted to voluntarily participate in the study signed a consent form and were allowed to withdraw from the study any time. To ensure confidentiality, data were recorded in logbook using anonymous codes.

RESULTS

Demographic characteristics of people living with HIV/AIDS seen at one primary healthcare facility in Rwanda.

The current study has recruited and included 417 participants who were HIV positive. Female and male patients were 41.3% and 58.7%, respectively, and there was no statistical significant difference between genders (*P* value 0.7). The age-groups of 31–40 and 41–50 years were more predominant, with 27.6% and 26.4%, respectively, and there was a statistical significant difference between the age-groups among the study participants (*P* value 0.0003) (Table 1).

Prevalence of HIV/HCV coinfection among the study participants.

Among 417 participants, 52 were screened to be HCV positive (12.5%). Among all age-groups, the group of 41- to 50- and 51- to 60-year-olds exhibited high percentage of HIV/HCV coinfection, with 3.6% and 4.6%, respectively, compared with other age-groups. However, there was no statistical significant difference of having comorbidities among all age-groups, *P* value 0.9 (Table 2).

Comorbidities among the study patients. We have also evaluated comorbidities among all 417 study participants. Forty-two of 52 (80.7%) patients with HIV/HCV coinfection had comorbidities and 72 of 365 (19.7%) HIV mono-infection had co-morbidities. In general, five comorbidities were observed, including hypertension 8.4%, diabetes mellitus 8.2%, liver damage 4.8%, renal failure 4.3%, and active tuberculosis (TB) disease 1.5%. Moreover, the patients with HIV/HCV coinfection had increased risk of having comorbidities with an RR of 4.09 (Table 3).

DISCUSSION

The current study has evaluated the prevalence of HIV/HCV coinfection and associated comorbidities. Generally, the prevalence of HIV/HCV coinfection in this study was 12.5%. This is in line with a systematic review conducted in sub-Saharan Africa which showed a pooled seroprevalence of 11–87% of HIV/HCV coinfection across all high-risk groups.^{14,15} However, a previous countrywide study conducted in Rwanda in 30 antenatal clinics among pregnant women living with HIV showed lower percentage of HIV/HCV coinfection of 3.9%.¹⁶ A similar study conducted by

TABLE 2

HCV sero prevalence in people living with HIV/AIDS in Rwanda distributed by age-group and gender

Age-group (years)	Male	Female	Total	P-value
≤ 20	0 (0)	0 (0)	0 (0)	0.9
21–30	1 (0.2)	3 (0.7)	4 (0.96)	
31–40	2 (0.5)	3 (0.7)	5 (1.2)	
41–50	6 (1.5)	9 (2.2)	15 (3.6)	
51–60	9 (2.2)	10 (2.4)	19 (4.6)	
≥ 61	5 (1.2)	4 (1.0)	9 (2.2)	
Total	20 (4.80)	32 (7.7)	52 (12.5)	

HCV = Hepatitis C virus. The Prevalence of HIV/HCV coinfection. Data are presented as frequency (%) unless otherwise indicated. *P* value less than 0.05 was considered statistically significant (*n* = 417).

TABLE 3
Comorbidities in people living with HIV/AIDS and people with HCV/HIV coinfection in Rwanda

Variables	Liver damage (%)		Active tuberculosis disease (%)		Renal failure (%)		Hypertension (%)		Diabetes mellitus (%)		Total (%)	
	HIV mono-infected (N = 365)	HIV/HCV coinfectd (N = 52)	HIV mono-infected (N = 365)	HIV/HCV coinfectd (N = 52)	HIV mono-infected (N = 365)	HIV/HCV coinfectd (N = 52)	HIV mono-infected (N = 365)	HIV/HCV coinfectd (N = 52)	HIV mono-infected (N = 365)	HIV/HCV coinfectd (N = 52)	HIV mono-infected (N = 365)	HIV/HCV coinfectd (N = 52)
Male	5 (1.4)	3 (5.7)	2 (0.5)	1 (1.9)	5 (1.4)	2 (3.8)	11 (3.0)	5 (9.6)	4 (1.0)	8 (15.3)	28 (7.7)	19 (36.5)
Female	10 (2.7)	2 (3.8)	2 (0.5)	1 (1.9)	8 (2.2)	3 (5.7)	15 (4.1)	4 (7.7)	9 (2.5)	13 (25.0)	44 (12.0)	23 (44.2)
Subtotal	15 (4.1)	5 (9.6)	4 (1.1)	2 (3.8)	13 (3.5)	5 (9.6)	26 (7.1)	9 (17.3)	13 (3.5)	21 (40.38)	72 (19.7)	42 (80.7)
P-value	0.005		0.005		0.003		0.001		0.001		0.001	
RR	4.09											

HCV = Hepatitis C virus; RR = relative risk. Comparison of the frequency of comorbidities in HIV-mono-infected patients and HIV/HCV-coinfection patients: Data are presented as frequency (%) unless otherwise indicated. The prevalence of complication was calculated among HIV-mono-infected and HIV/HCV-coinfection participants. The RR of having comorbidities was calculated. P value less than 0.05 was considered statistically significance ($n = 417$) ($n = 365$ for HIV-mono-infected patients and $n = 52$ for HIV/HCV-coinfection patients).

Umumararungu et al. in Rwanda has found a higher percentage of HIV/HCV coinfection of 28.4%.¹⁷ Another study also conducted in Rwanda showed a prevalence of 4.6% of HIV/HCV coinfection.¹⁸ This prevalence variation in Rwanda may be associated with recruited participants, samples size, age of participants, geographic region, and mode of transmission, as previously suggested.^{13,19} Moreover, this discordance of data in the same country suggests a large-scale multicenter study to establish the exact prevalence.

In the current study, we have found that age-groups of 41–50 and 51–60 years were more affected than other age-groups, with the prevalence of 3.6% and 4.6%, respectively. This is in accordance with the conclusion of Umutesi et al., a study conducted in Rwanda previously, concluded that increased age might be one of the factors, which influence HCV infection.¹⁸ With regard to the gender, in our study, there was no statistical significant difference between male and female participants (P value 0.7). However, among HIV/HCV-coinfection participants, female individuals were more affected than male patients, with 7.7% and 4.8%, respectively. This is similar to the recent study conducted by Jemilohun et al. in the southwestern region of Nigeria, showing a higher HIV/HCV coinfection prevalence in female patients 0.4% than male patients 0.4%.²⁰

A higher prevalence of HCV among male subjects was reported in the study conducted by Tremeau et al., a study evaluating the seroprevalence of hepatitis B and C infections among the HIV-positive population in Abuja, Nigeria, which was 3.5% in male patients and 1.2% in female patients.²¹ This discrepancies and controversial data may be due to geographical distribution, sample size, and recruited participants.

We have also evaluated comorbidities among the study participants; hypertension, diabetes mellitus, liver damage, renal failure, and active TB disease were the observed comorbidities. The group of HIV/HCV coinfections exhibited an increased risk of having comorbidities compared with the group of HIV mono-infection. A similar study conducted by Rossi et al. has found that HCV coinfection is associated with an increased risk of incident chronic kidney disease in HIV-infected patients.²² A systematic review conducted in sub-Saharan Africa showed that risk factors for pharmacological toxicity are numerous and depend mainly on underlying patients' characteristics and the drug regimen under consideration in HIV/HCV-coinfection patients. In their review, they highlight that patients' age, gender, body weight and size, nutrition, and overall health status can play a role in how one experiences side effects because of one's immune status.¹⁴ In our study, we have found that coinfection patients have an

increased risk of having comorbidities than mono-infected patients. This high percentage could be associated with their depleted immunity. Therefore, more studies are needed to evaluate and compare immune status of HIV/HCV-coinfection and HIV-mono-infected patients and appropriate intervention.

LIMITATION

The current study had a small sample size and positive cases were not confirmed by PCR. Further study with large sample size should consider this for establishment of exact prevalence of HIV/HCV coinfection in Rwanda.

CONCLUSION

This study gives an update on the prevalence of HIV/HCV coinfection of 12.5% and percentages of comorbidities, which include hypertension, diabetes mellitus, liver damage, renal failure, and active TB disease. In addition, the current study highlights an increased risk of having comorbidities in HIV/HCV-coinfection patients including liver toxicity, renal failure, hypertension, and diabetes mellitus. These findings suggest the need for more intervention to protect this high-risk group of people.

Received May 18, 2020. Accepted for publication January 24, 2021.

Published online March 15, 2021.

Acknowledgments: We sincerely thank the authority of the Remera Health center for allowing us to carry out this study. The American Society of Tropical Medicine and Hygiene (ASTMH) assisted with publication expenses.

Authors' addresses: Jean Bosco Munyemana, Department of Clinical Biology, School of Medicine and Pharmacy, College of Medicine and Health Sciences, University of Rwanda, Kigali, Rwanda, E-mail: munyebos1@gmail.com. Esperance Mukanoheli, Department of Biomedical Laboratory Sciences, Faculty of Applied Fundamental Sciences, INES-Ruhengeri, Musanze, Rwanda, E-mail: esperancemukanoheli98@gmail.com. Theoneste Nsabimana, Department of Internal Medicine, Kibagabaga District Hospital, Kigali, Rwanda, E-mail: nsabitheo@gmail.com. Jean Damascene Niringiyumukiza, Department of Obstetrics and Gynecology, Reproductive Endocrinology and Infertility Clinic, Rwanda Military Hospital, Kigali, Rwanda, E-mail: nidamas2000@yahoo.fr.

REFERENCES

1. Chung RT, Baumert TF, 2014. Curing chronic hepatitis C--the arc of a medical triumph. *N Engl J Med* 370: 1576–1578.
2. Mohamed AA, Elbedewy TA, El-Serafy M, El-Toukhy N, Ahmed W, Ali El Din Z, 2015. Hepatitis C virus: a global view. *World J Hepatol* 7: 2676–2680.

3. Rockstroh JK et al., 2015. Efficacy and safety of grazoprevir (MK-5172) and elbasvir (MK-8742) in patients with hepatitis C virus and HIV co-infection (C-EDGE CO-INFECTION): a non-randomised, open-label trial. *Lancet HIV* 2: e319–e327.
4. Tovo PA, Calitri C, Scolfaro C, Gabiano C, Garazzino S, 2016. Vertically acquired hepatitis C virus infection: correlates of transmission and disease progression. *World J Gastroenterol* 22: 1382–1392.
5. Frias M, Rivero-Juarez A, Lopez-Lopez P, Rivero A, 2018. Pharmacogenetics and the treatment of HIV-/HCV-coinfected patients. *Pharmacogenomics* 19: 979–995.
6. Raja R, Baral S, Dixit NM, 2018. Interferon at the cellular, individual, and population level in hepatitis C virus infection: its role in the interferon-free treatment era. *Immunol Rev* 285: 55–71.
7. Thomas DL, Leoutsakas D, Zabransky T, Kumar MS, 2011. Hepatitis C in HIV-infected individuals: cure and control, right now. *J Int AIDS Soc* 14: 22.
8. Platt L, Easterbrook P, Gower E, McDonald B, Sabin K, McGowan C, Yanny I, Razavi H, Vickerman P, 2016. Prevalence and burden of HCV co-infection in people living with HIV: a global systematic review and meta-analysis. *Lancet Infect Dis* 16: 797–808.
9. Rouet F et al., 2004. HBV and HCV prevalence and viraemia in HIV-positive and HIV-negative pregnant women in Abidjan, Cote d'Ivoire: the ANRS 1236 study. *J Med Virol* 74: 34–40.
10. Luma HN, Eloumou SA, Ekaney DS, Lekpa FK, Donfack-Sontsa O, Ngahane BH, Mapoure YN, 2016. Sero-prevalence and correlates of hepatitis B and C Co-infection among HIV-infected individuals in two regional hospitals in Cameroon. *Open AIDS J* 10: 199–208.
11. Onakewhor JU, Okonofua FE, 2009. The prevalence of dual human immunodeficiency virus/hepatitis C virus (HIV/HCV) infection in asymptomatic pregnant women in Benin City, Nigeria. *Afr J Reprod Health* 13: 97–108.
12. Askari A, Hakimi H, Nasiri Ahmadabadi B, Hassanshahi G, Kazemi Arababadi M, 2014. Prevalence of hepatitis B Co-infection among HIV positive patients: narrative review article. *Iran J Public Health* 43: 705–712.
13. Wei Y, Li W, Du T, Hong Z, Lin J, 2019. Targeting HIV/HCV coinfection using a machine learning-based multiple quantitative structure-activity relationships (multiple QSAR) method. *Int J Mol Sci* 20: 3572.
14. Koziel MJ, Peters MG, 2007. Viral hepatitis in HIV infection. *N Engl J Med* 356: 1445–1454.
15. Rao VB, Johari N, du Cros P, Messina J, Ford N, Cooke GS, 2015. Hepatitis C seroprevalence and HIV co-infection in sub-Saharan Africa: a systematic review and meta-analysis. *Lancet Infect Dis* 15: 819–824.
16. Mutagoma M, Balisanga H, Sebuho D, Mbituyumuremyi A, Remera E, Malamba SS, Riedel DJ, Nsanzimana S, 2017. Hepatitis C virus and HIV co-infection among pregnant women in Rwanda. *BMC Infect Dis* 17: 167.
17. Umumamarungu E, Ntaganda F, Kagira J, Maina N, 2017. Prevalence of hepatitis C virus infection and its risk factors among patients attending Rwanda military hospital, Rwanda. *Biomed Res Int* 2017: 5841272.
18. Umutesi J, Simmons B, Makuza JD, Dushimiyimana D, Mbituyumuremyi A, Uwimana JM, Ford N, Mills EJ, Nsanzimana S, 2017. Prevalence of hepatitis B and C infection in persons living with HIV enrolled in care in Rwanda. *BMC Infect Dis* 17: 315.
19. Kuehlkamp VM, Schuelter-Trevisol F, 2013. Prevalence of human immunodeficiency virus/hepatitis C virus co-infection in Brazil and associated factors: a review. *Braz J Infect Dis* 17: 455–463.
20. Jemilohun AC, Oyelade BO, Oiwoh SO, 2014. Prevalence of hepatitis C virus antibody among undergraduates in ogbomos, southwestern Nigeria. *Afr J Infect Dis* 8: 40–43.
21. Tremereau-Bravard A, Ogbukagu IC, Ticao CJ, Abubakar JJ, 2012. Seroprevalence of hepatitis B and C infection among the HIV-positive population in Abuja, Nigeria. *Afr Health Sci* 12: 312–317.
22. Rossi C et al., 2017. Hepatitis C co-infection is associated with an increased risk of incident chronic kidney disease in HIV-infected patients initiating combination antiretroviral therapy. *BMC Infect Dis* 17: 246.