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Seroprevalence and associated risk factors of hepatitis C infection among diabetic patients in South-Kivu, Eastern Democratic Republic of the Congo: A cross-sectional study

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Abstract

Background and Aims: Hepatitis C virus (HCV) infection and diabetes mellitus (DM) are two frequent diseases in the Democratic Republic of the Congo (DRC) and several studies seem to show a link between the two diseases worldwide. However, no study has evaluated this link in our country. The present study aimed at determining the seroprevalence of HCV in diabetic patients as well as associated risk factors.

Methodology: A multicenter cross-sectional study allowed us to sample diabetic patients in two diabetic healthcare centers of Bukavu city in the eastern part of the DRC, from December 2020 to December 2022. A questionnaire was submitted to the diabetic patients to collect sociodemographic data, anamnestic data on risk factors for HCV infection, and clinical data on DM. These factors were analyzed based on anti-HCV serological results.

Results: Among the 180 selected patients, 19 (10.6%) were tested positive for anti-HCV antibodies. After multivariate analysis, the identified factors influencing these outcomes were male sex (adjusted odds ratio [aOR]: 3.5, $p = 0.027$), dental extraction (aOR: 7.6, $p = 0.001$), and living in a privileged environment (aOR: 0.29, $p = 0.03$). The factors related to DM such as the type, the disease duration, or the usual type of treatment did not influence the serological results.

Conclusion: This study shows that HCV seroprevalence in diabetic patients is very high compared with the general population. This suggests combined screening and management policies in this population.

KEYWORDS

diabetes mellitus, DRC, Hepatitis C virus, seroprevalence

1 | INTRODUCTION

Diabetes mellitus (DM) and viral hepatitis are significant public health problems globally. DM is a metabolic disease characterized by chronic hyperglycemia resulting from a defect in insulin secretion or impaired insulin action. It affects approximately 8.5% of the world's population aged 18 years or older and was directly responsible for 1.5 million deaths in 2019.[1,2]

Hepatitis C virus (HCV) infection is a major cause of chronic liver disease, leading to cirrhosis or hepatocellular carcinoma. In 2019, it affected 58 million people worldwide and caused 400,000 deaths.[3]

Several studies have reported a link between DM and HCV infection.[4–6] Diabetic patients are more susceptible to HCV transmission due to repeated injections and needles, especially when performed in poor conditions. Conversely, HCV infection can cause insulin resistance, leading to DM.[7] However, the direct causal link remains unclear. This association is concerned with uncontrolled Type 2 DM, which leads to progression of hepatic steatosis to non alcoholic steatohepatitis, which may increase the risk of hepatic cirrhosis during chronic HCV infection.[8]

Therefore, even if special screening of HCV in diabetic people is not commonly recommended, early detection of HCV infection seems to be crucial since early eradication of this virus could prevent liver complications and improve insulin resistance in type 2 DM.[9] The development of direct-acting antivirals has made HCV eradication possible, with a success rate close to 100%.[10] However, the high cost of this treatment limits its availability, particularly in sub-Saharan African countries, where only 13% of individuals with chronic hepatitis worldwide receive treatment.[3]

This worrying situation, therefore, justifies the screening of both HCV and the associated factors that may influence the presence of this virus during DM and the implementation of effective preventive measures, especially for developing countries.

Most African countries are going through an epidemiological transition period characterized by the coexistence of noncommunicable diseases such as DM and infectious diseases such as HCV infection. The prevalence of DM and HCV is not well known in the Democratic Republic of the Congo (DRC), which, however, is ranked among the most affected African countries. A meta-analysis by Riou et al. had estimated the prevalence of HCV at 2.4% while another systematic review found 2.9%.[11,12] DM prevalence in some population groups in the country is estimated to range from 2.8% to 17.7%.[13,14] Given the high prevalence of both diseases in the DRC and the potential risk of co-occurrence, evaluating the extent of their link is necessary. To our knowledge, no study has assessed this issue in the country. Therefore, the aim of this study was to determine HCV seroprevalence in diabetic patients and identify potential risk factors for HCV infection in DM.

Key points

- What's Known: Hepatitis C infection remains common in diabetics people.
- What's new: Male sex and dental extraction would be favoring factors of this infection among diabetic people. Living in a privileged environment would have a protective effect.
- Clinical implications: Systematic screening and preventing measures for this infection are very important among diabetics.

2 | PATIENTS AND METHODS

2.1 | Study design

This bi-centric study took place in two healthcare facilities, including a secondary care center and a tertiary hospital in the city of Bukavu in the eastern part of the DRC. The research was conducted from December 2020 through December 2022.

During the study period, we consistently interviewed all previously known or newly diagnosed diabetic patients who were consulted or received follow-up care in the two research facilities. All types of DM patients were included. As a result, we enrolled 180 patients in the two care centers (convenience sample size).

In both hospitals, DM diagnosis was confirmed through documented use of oral antidiabetic drugs (OADs) or insulin, a random blood glucose level exceeding 200 mg/dL associated with clinical manifestations, or a fasting blood glucose level above 126 mg/dL on two separate occasions using American Diabetes Association criteria.[15] Additionally, the selected patients were given a questionnaire to gather sociodemographic data, anamnestic information on risk factors for HCV infection, and clinical data related to DM.

We excluded pregnant patients and diabetics who declined to answer our questionnaire or provide a blood sample.

2.2 | Sample collection and antibody detection

Blood samples were collected using a sterile needle, stored in a sterile ethylene diamine tetraacetic acid tube, and promptly transported to the lab. Each participant provided 3 mL of venous blood, immediately centrifuged upon arrival.

Anti-HCV antibody screening was conducted with a high-performance rapid immunochromatographic kit (FaStep Polymed Therapeutics ©), boasting near 100% sensitivity and specificity. Results were interpreted following the manufacturer's guidelines.

Positive cases were verified using a third-generation ELISA kit (Lab kit Chemelex©, S.A.) for quantitative detection of anti-HCV antibodies.

Due to limited resources, the baseline liver function tests could not be performed.

2.3 | Statistical analysis

The collected data for this study were compiled into Excel spreadsheets and subsequently subjected to rigorous analysis using

IBM SPSS Statistics 26. The homogeneity of variances for continuous variables was assessed using the Kolmogorov–Smirnov normality test. The data are presented as a frequency or median ± standard deviation.

χ^2 or Fisher's exact tests were used to compare categorical variables, while continuous variables were examined using the Student's *t* test. For non-normally distributed variables, the robust Wilcoxon test served as an alternative to the *t* test. A two-sided *p*-value of <0.05 was established as the threshold for statistical significance. Bivariate and multivariate logistic regression models were built to identify risk factors associated with viral hepatitis in diabetic patients.

2.4 | Ethical considerations

Following the detailed explanation of the objectives and methodology of this study, written informed consent was obtained from participants before data collection and blood sample acquisition. This research was granted approval by the Faculty of Medicine at the Official University of Bukavu (N°UOB-SK/FM/SECAF/CBY/009/2020), as well as by the authorities of the Center Charles Mbogha. The patients who tested positive for HCV were directed to a hepatologist for complimentary consultations.

3 | RESULTS

3.1 | General characteristics

Out of the 180 patients who participated in this study, 142 (78.9%) were women. The mean age of the participants was 58.2 ± 12.8 years, with the majority of subjects being aged 50 years and older (77.2%).

Educationally, the majority of patients had an average level of secondary school education, which was reported in approximately 42.2% of cases. A similar trend was observed for the educational level of their spouses. Additionally, 68.3% of patients had a body mass index (BMI) above 25 kg/m^2.

With regard to DM, type 2 diabetes was more prevalent (87.8%), and the majority of the patients had disease duration of less than 5 years (42%). Their usual treatment included OADs in 61.7% of cases. Regarding viral serology, 19 out of the 180 patients (10.9%) tested positive for HCV antibodies (Table 1).

3.2 | Risk factors for HCV acquisition

In this study, the patients reported the following factors: blood transfusion (17.8%), tattooing (30.6%), dental extraction (40.0%), being healthcare practitioners (3.3%), and previous surgery (41.7%). Among these factors, only dental extraction appeared to have a significant link with HCV seropositivity (19.4% vs. 4.6%, $p = 0.002$), as demonstrated in Table 2.

TABLE 1 General characteristics of the study population and their influence on the HCV serological result.

		Serologic results		
	Total *n* (%)	HCV-negative	HCV-positive	*p* value
		161 (89.4)	19 (10.6)	
Age range, *N* (%)				
<20	5 (2.8)	5 (100)	0 (0)	
20–50	36 (20.0)	33 (91.7)	3 (8.7)	
>50	139 (77.2)	123 (88.5)	16 (11.5)	0.63
Gender, *N* (%)				
F	142 (78.9)	131 (92.3)	11 (7.7)	
M	38 (21.1)	30 (78.9)	8 (21.1)	0.02
BMI, *N* (%)				
<18	8 (4.4)	6 (75)	2 (25)	
18–24.99	48 (26.7)	43 (89.6)	5 (10.4)	
≥25	124 (68.3)	112 (90.3)	12 (9.3)	0.39
Residence, *N* (%)				
Bagira commune	13 (7.2)	11(84.6)	2 (15.4)	0.56
Ibanda commune	90 (50.0)	86 (95.6)	4 (4.4)	0.03
Kadutu commune	63 (35.0)	53 (84.1)	10 (15.9)	0.09
Rural	13 (7.2)	10 (76.9)	3 (23.1)	0.08
Study level, *N* (%)				
Primary	44 (24.4)	39 (88.6)	5 (11.4)	
Secondary	76 (42.2)	69 (90.8)	7 (9.2)	
University	17 (9.4)	14 (82.4)	3 (11.6)	
No level	43 (23.9)	39 (90.7)	4 (9.3)	0.76
Spouses level of study, *N* (%)				
Primary	14 (7.8)	13 (92.9)	1 (7.1)	
Secondary	76 (42.2)	68 (89.5)	8 (10.5)	
University	44 (24.4)	40 (90.9)	4 (9.1)	
No level	46 (25.6)	40 (87.0)	6 (13)	0.90
Types of diabetes, *N* (%)				
T1	22 (12.2)	19 (86.4)	3 (13.6)	
T2	158 (87.8)	142 (89.9)	16 (10.1)	0.61
Diabetes duration (%)				
<5	76 (42.2)	68 (89.5)	8 (10.5)	
>10	33 (18.3)	29 (87.9)	4 (12.1)	
5–10	71(39.4)	64 (90.1)	7 (9.9)	0.94
Usual treatment, *N* (%)				

(Continues)

TABLE 1 (Continued)

	Total *n* (%)	Serologic results: HCV-negative	Serologic results: HCV-positive	*p* value
OAD	111 (61.7)	101 (91.0)	10 (9)	
Insulin	62 (34.4)	55 (88.7)	7 (11.3)	
Hygienic and dietary measures only	7 (3.9)	5 (71.4)	2 (28.6)	0.25

Abbreviations: BMI, body mass index; HCV, Hepatitis C virus; OAD, oral antidiabetic drugs.

TABLE 2 Risk factors for HCV and their influence on serological results.

Potential risk factors	Total *n* (%)	Serologic results: HCV negative	Serologic results: HCV positive	*P* value
		161 (89.4)	19 (10.6)	
Blood transfusion				
No	148 (82.2)	135 (91.2)	13 (8.8)	
Yes	32 (17.8)	26 (81.3)	6 (18.8)	0.09
Tatoos				
No	125 (69.4)	110 (88.0)	15 (12.0)	
Yes	55 (30.6)	51 (92.7)	4 (7.3)	0.34
Dental extraction				
No	108 (60.0)	103 (95.4)	5 (4.6)	
Yes	72 (40.0)	58 (80.6)	14 (19.4)	0.002
Surgery				
No	105 (58.3)	96 (91.4)	9 (8.6)	
Yes	75 (41.7)	65 (86.7)	10 (13.3)	0.30
Healthcare practitioners				
No	174 (96.6)	156 (89.7)	18 (10.3)	
Yes	6 (3.3)	5 (83.3)	1 (16.6)	0.49

Abbreviation: HCV, Hepatitis C virus.

Bivariate analysis revealed that male gender increased the risk of testing positive for HCV by three times (odds ratio [OR]: 3.1, $p = 0.0023$), and dental extraction increased the risk by approximately five times (OR: 4.9, $p = 0.003$). However, residing in Ibanda commune was associated with a protective effect (OR: 0.2, $p = 0.013$).

In multivariate analysis, the protective effect of living in the Ibanda commune was conserved (adjusted odds ratio [aOR]: 0.26, 95% confidence interval [CI]: 0.08–0.87, $p = 0.03$) while male sex and a history of dental extraction continued to show significant association with HCV seropositivity, with aOR values of 3.5 ($p = 0.027$) and 7.6 ($p = 0.001$), respectively (refer to Table 3).

4 | DISCUSSION

This cross-sectional study aimed at determining the seroprevalence of HCV in diabetic patients and investigating potential associated factors. Our study revealed a seroprevalence of 10.6%, with male gender and dental extraction found to be risk factors.

The prevalence of HCV in sub-Saharan Africa was estimated to be 3% in a systematic review and a meta-analysis conducted in 2015.[16] In the DRC, only data from specific subpopulations are available. In a large cohort study by Mudji et al., the prevalence was found to be 3% in volunteer blood donors and 10.5% in patients with suspected liver disease.[17] Another study by Kabinda et al. found a seroprevalence of 4.1% in pregnant women.[18] Although the overall prevalence of HCV in the DRC remains unknown, a systematic review of studies conducted on various population groups estimated it to be around 2.9%.[11] The prevalence found in our study, which is 11%, is higher than the overall estimates, but similar to a similar study conducted in Congo-Brazzaville.[19]

In a Chinese study conducted by Hua-Fen Chen et al., HCV prevalence was found to be three times higher in diabetic patients compared with nondiabetics, while a Turkish study by Okan et al. found a prevalence of 7.5% in diabetic patients compared with 0.1% in nondiabetics.[20,21] That high frequency could be explained by the association between hepatitis C, hepatic steatosis, and excessive production of tumor necrosis factor. This latter may favor insulin resistance and subsequent type 2 DM.[8] DM is also more common in patients with HCV than in patients with other chronic liver diseases, such as viral hepatitis B.[5] This suggests a peculiarity of HCV

TABLE 3 Logistic regression of factors influencing serological results.

	Bivariate analysis: OR	95% CI	*p* value	Multivariate analysis: adjusted OR	95% CI	*p* value
Male sex	3.1	1.1–8.5	0.024	3.6	1.2–10.7	0.02
Ibanda commune	0.2	0.07–0.73	0.039	0.26	0.08–0.87	0.03
Kadutu commune	2.26	0.6–5.5	0.095	-	-	-
Blood transfusion	2.3	0.8–6.8	0.104	-	-	-
Dental extraction	4.9	1.7–14.5	0.003	5.6	1.8–17.4	0.003

concerning DM, and studies have incriminated genotype 3 in inducing more hepatic steatosis.[7] HCV may also interfere with GLUT 1 and 2 receptors, disrupting glucose absorption. Experimental studies have also shown that HCV may be involved in the regulation of phosphorylation of insulin receptor substrate 1 (IRS-1).[22] Another study showed how improving insulin-resistance parameters, such as BMI, could positively influence the response to antiviral therapy for HCV infection.[23]

In the present study, we also investigated conditions influencing HCV infection. Three factors were found to be associated with serological results: male gender, dental extraction, and living in Ibanda Commune. Male gender and dental extraction increased the risk of HCV infection by 3.5 and 7.2 times, respectively. While several studies have not found an influence of sex in the occurrence of HCV infection in diabetic patients,[4,5,18,24] other studies have shown a higher prevalence of HCV in male patients of some subgroups of nondiabetic patients.[25] Nevertheless, men are traditionally more exposed to certain transmission factors, such as tattoos and scarification.[26] However, the possible male gender influence found in our study should be interpreted with caution since females represent almost 80% of our patients. This could be a selection bias.

As found in our study, dental extraction is recognized as a risk factor for viral hepatitis C in the general population of developing countries.[27] Living in Ibanda commune seems to be protective (aOR:0.26, $p = 0.03$). This may be explained by the high living standard of the population in this commune as well as the high accessibility to healthcare services compared with the other two communes of the city of Bukavu.

5 | CONCLUSION

Our study shows that HCV antibodies are common in diabetic patients, emphasizing the need for systematic screening of new cases. Early identification and management of HCV in diabetic patients can improve prognostic outcomes. Male patients and those with a history of dental extraction are at higher risk, so healthcare providers should consider these factors when developing screening and management strategies. Our study highlights the importance of comprehensive protocols for optimizing health outcomes in diabetic patients with HCV antibodies.

6 | LIMITATIONS

Our study is limited by the type of sampling and the small sample size, which prevents us from generalizing our findings to all diabetics in our region. Furthermore, the failure of PCR to confirm the activity of the virus may have affected the interpretation of our results, potentially including former carriers of HCV. Additionally, due to financial constraints, we were unable to assess parameters related to baseline liver function or the level of diabetes control through glycated hemoglobin rates. A prospective study that incorporates these parameters would be beneficial in evaluating the relationship between these diseases and the impact of their level of activity/control on each other. Finally, no formal sample size calculation has been performed and selection bias cannot be ruled out.

AUTHOR CONTRIBUTIONS

Yannick Chibinda Birato: Data curation; formal analysis; writing—original draft; Writing—review & editing. **Tony Akilimali Shindano**: Conceptualization; formal analysis; methodology; project administration; writing—review & editing. **Daudi Cinyabuuma**: Data curation. **Ciza Abel**: Conceptualization; data curation. **Cikomola Justin Chiruza**: Writing—review & editing. **Andre N. H. Bulabula**: Writing—review & editing.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are openly available in Mendeley Data at https://data.mendeley.com/datasets/495334579x/1 (doi: 10.17632/495334579x.1).

TRANSPARENCY STATEMENT

The lead author Tony Akilimali Shindano affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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