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ORIGINAL RESEARCH

Impact of Sexualized Substance Use and Other Risk Practices on HCV Microelimination in gbMSM Living with HIV: Urgent Need for Targeted Strategies. Results of a Retrospective Cohort Study

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ABSTRACT

Introduction: The objective of the present study is to describe the incidence of recently acquired hepatitis C (RAHCV) in a large cohort of people living with HIV (PLWHIV) and sexualized drug use and other related risk behaviours.

Methods: Observational study including all PLWHIV with a RAHCV episode between June 2005 and December 2019 at the Hospital Clinic of Barcelona, Spain. Incidence of RAHCV was determined per person calendar year (py) in those patients who were HCV RNA negative. Data were collected on high-risk sexual practices for HCV transmission focused on gay, bisexual and other men having sex with men (gbMSM).

Results: A total of 340 RAHCV were diagnosed in 290 PLWHIV; 274 (94%) of them were gbMSM and developed 324 RAHCV, mainly since 2010 (90%). Overall incidence rate (IR) of RAHCV in gbMSM was 0.10 py (95% CI 0.09–0.11), with a 40% decreased observed since 2017 (IR 0.06, 95% CI 0.03–0.09 in 2019). Sixty reinfections were detected in 50 gbMSM (*n* = 244, 20%). The overall reinfection IR was 0.17 per py (95% CI 0.12–0.23) and the proportion of reinfection among total RAHCV increased to 47% cases in 2019, mainly in patients engaged in sexualized substance use (76%), unprotected anal intercourse (94%), sex partying (80%), fisting (43%), slamming (14%) and 60% of concomitant sexually transmitted infections (STIs).

Conclusions: Despite RAHCV incidence decline in our cohort since 2017, HCV reinfection increased. High sexualized substance use and other risk behaviours are described in this context, indicating the need for public health tailored strategies to reduce this transmission and achieve HCV microelimination in gbMSM living with HIV.

Keywords: Sexualized substance use; HCV; HIV; Incidence; GbMSM; Reinfection

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Key Summary Points

The present article describes our institutional experience of more than 15 years in recently acquired hepatitis C (RAHCV) among PLWHIV.

A total of 340 RAHCV were diagnosed in 290 PLWHIV; 274 (94%) of them were gbMSM and developed 324 RAHCV, mainly since 2010 (90%). A decrease of 40% in RAHCV incidence was observed since 2017, but the proportion of reinfection among total RAHCV increased to 47% cases in 2019, mainly in patients engaged in sexualized substance use, unprotected anal intercourse, sex partying, fisting, slamming and 60% of concomitant STIs.

Our results show the urgent need for public health tailored strategies to reduce this transmission and achieve HCV microelimination in gbMSM living with HIV.

DIGITAL FEATURES

This article is published with digital features, including a summary slide, to facilitate understanding of the article. To view digital features for this article go to https://doi.org/10.6084/m9.figshare.14393888.

INTRODUCTION

In recent years, increasing evidence of sexually transmitted hepatitis C virus (HCV) infection has emerged worldwide among gay, bisexual and other men who have sex with men (gbMSM) living with HIV. Evidence is growing that the incidence of HCV infection is increasing in this group [1] but also the potential for HCV reinfection. The observed high rates of new infections have negative health consequences and compromise the efforts to limit the HCV epidemic and achieve the World Health Organization (WHO) elimination goals of reducing infections by 80% and mortality by 65% by 2030 [2].

Our centre was among the first to document the epidemic outbreak of acute hepatitis C infection among MSM living with HIV in Barcelona, Spain [3–6]. This trend has continued with the diagnosis of approximately 35 new episodes per year, of which an increasing number were reinfections. Of note, the NEAT consensus panel has recently proposed the use of the term "recently acquired hepatitis C infection" (RAHCV) to replace the term "acute hepatitis C infection" and the reasoning for the new terminology is discussed in detail in the corresponding publication [7]. In the era of expanded use of direct-acting antiviral agents (DAA) for chronic HCV infection, with the consequent decrease of HCV transmitters [8] and a global decline in HCV incidence, suggesting the effect of treatment-as-prevention strategy, is essential to expand current knowledge on HCV infection and reinfection in gbMSM living with HIV, mainly because a high incidence of HCV is still observed in this population compared to other populations [9–12].

Further, there is a need to characterize risk factors of HCV infection amongst gbMSM, and potential predictors for reinfection, with a special focus on the "chemsex" phenomenon, a subset of sexualized drug use to enhance sexual experience that emerged in modern gay culture around the world; and how the practice is impacting sex pleasure and sexual health in the community [13]. Studies have shown that people engaged in chemsex are more likely to engage in higher-risk sexual practices such as having sex with multiple partners, fisting and sharing sex toys, slamsex (injecting chemsex drugs), and to be diagnosed with concomitant sexually transmitted infections (STIs) [14–17]. This is worrisome, since all of these sexual behaviours associated with chemsex may facilitate the ongoing spread of HCV in this population [18].

The aim of the present article is to describe our institutional experience over 15 years in RAHCV among people living with HIV

(PLWHIV), while highlighting the alarming incidence of reinfection, mainly in gbMSM, and the influence that sexualized drug use may have, among other vulnerability factors. A better understanding of the sexual risk factors related to HCV infection and reinfection is needed to implement public health strategies to prevent sexually transmitted HCV. To the best of our knowledge, the Hospital Clinic of Barcelona has the largest Spanish cohort of PLWHIV with almost 6000 patients on follow-up. The subset of 63% describing themselves as gbMSM is one of the largest cohorts in Europe. This centre is in an area with a large gay community, which contributes to the higher detection rate of HCV episodes among gbMSM compared with other centres.

METHODS

We included all PLWHIV who were diagnosed with RAHCV between June 2005 and December 2019 at the Hospital Clinic in Barcelona, Spain. The study was approved by the Hospital Clinic Ethics Committee and all patients gave their written informed consent to use their data for health research purposes.

PLWHIV in our centre were routinely followed up every 6 months. Testing for antibodies to HCV was requested at diagnosis of HIV and then every 2 years, or more frequently (every 6 months or less) in case of high-risk HCV infection behaviours.

RAHCV was defined as positive anti-HCV IgG and a documented negative anti-HCV IgG in the previous 12 months OR positive HCV-RNA and a documented negative HCV-RNA or negative anti-HCV IgG in the previous 12 months.

In addition, patients with evidence of symptomatic infection or unexplained increase in alanine aminotransferase were examined to rule out RAHCV. If diagnosis was confirmed, patients were followed and treated as per current clinical guidelines. To estimate the date of primary infection and confirm RAHCV, all plasma samples available 12 months before diagnosis were tested for HCV antibodies and HCV-RNA. Incidence of recently acquired infection was determined each calendar year in the subgroups of patients who were HCV RNA negative, considering that subjects with a negative HCV RNA in a specific year were at risk during the whole year. Until December 2016, all RAHCV episodes were treated with peginterferon plus ribavirin. As of January 2017, patients were started on DAA regimens.

We defined spontaneous HCV clearance as at least two HCV RNA detections 12 weeks apart, without having undergone any specific HCV treatment.

HCV reinfection was defined as detectable HCV-RNA after achieving a sustained virological response (SVR) 12 weeks after the end of treatment or following a spontaneous clearance, or HCV infection with a different genotype/subtype regardless of the period. Follow-up time at-risk for reinfection started at the end of HCV treatment for patients achieving SVR, and at the time of the second negative HCV-RNA for patients who spontaneously cleared their infection. And it ended when a reinfection was detected or on the last visit, whichever occurred first.

Data Collection

To screen HCV-infected patients, available plasma samples were tested for anti-HCV antibodies using the third-generation ADVIA Centaur HCV assay (Siemens Healthcare Diagnostics Inc. Tarrytown, NY 10591-5097, USA). Detection of HCV-RNA was performed with the Siemens VERSANT or the Roche Cobas® 6800 since 2017, both with a lower limit of quantification of 15 IU/mL to an upper limit of $1.0E + 08$ IU/mL (linear range). A real-time RT-PCR by restriction fragment length polymorphism (RFLP) was used to determine HCV genotypes.

Data on patient demographics, concomitant STIs, HCV infection, treatment history, symptoms, and virological and biochemical parameters were recorded. We also collected known risk behaviours for HCV transmission such as high-risk sexual practices (unprotected anal intercourse, fisting, sharing of sex toys, frequent casual sex with different partners) and

substance use in sexual context, including slam practices of injecting drug during sex.

Statistical Analysis

Socio-demographic, clinical and risk behaviour data were summarized using descriptive statistics. Quantitative variables were described with measures of central tendency and dispersion [mean (standard deviation), or median (interquartile range)], and qualitative variables with absolute (n) and relative (%) frequencies. Incidence of HCV infection and reinfection and 95% confidence intervals (CIs) were estimated using a Poisson regression model. Incidence rate ratio (IRR) was used to compare incidence rate (IR) between different periods. Data about sexual behaviour in gbMSM were available for the period 2018–2019, and associated risk factors were compared between individuals with acute HCV infection and those with reinfection using Fisher's exact test or chi-square test. All tests were two-tailed with a significance level of 0.05. Statistical analyses were conducted using Stata (StataCorp. 2017. Stata Statistical Software: Release 15. College Station, TX: StataCorp LLC).

RESULTS

Between June 2005 and December 2019, a total of 340 episodes of RAHCV were diagnosed in 290 PLWHIV, most of them (305 [90%] episodes in 256 patients) from 2010 onwards. Overall, 274 (94%) patients were gbMSM (median age of 39 years) and 4 (1.4%) people who inject drugs (PWID) out of sexual context. Of the 324 episodes reported within the cohort of 274 gbMSM, 293 episodes (90%) in 244 patients were reported from 2010 onwards (Fig. 1a). The overall IR of RAHCV in gbMSM was 0.09 (95% CI 0.08–0.10) during the study period and 0.10 (95% CI 0.09–0.11) from 2010 to 2019. Interestingly, the RAHCV IR decreased by 40% from 2017 (0.10, 95% CI 0.07–0.14) to 2019 (0.06, 95% CI 0.03–0.09), with an IRR of 0.60 (95% CI 0.34–1.07), coinciding with the introduction and generalization of DAA treatment. The main characteristics of RAHCV episodes and prescribed HCV treatment are shown in Table 1.

Information on recreational drug use was available for 85 of the 293 episodes (29%) diagnosed in gbMSM from 2010, of which 62 (73%) were diagnosed in a period of drug use during sex, mainly cocaine (30, 48%), GHB/GBL (30, 48%), methamphetamine (30, 48%), poppers (33, 53%), erection-enhancing medication (17, 27%), mephedrone (14, 23%) and ecstasy/MDMA (13, 21%). Sixty-five of these 293 episodes (22%) occurred concomitantly with other STIs, mainly syphilis (46, 71%), but also condyloma/human papillomavirus (HPV) (18, 28%), chlamydia and chlamydia/lymphogranuloma venereum (LGV) (14, 22%).

Hepatitis C Virus Reinfection

Of the 244 gbMSM diagnosed with HCV from 2010, 60 episodes of HCV reinfection were detected in 50 patients (20%), with an overall reinfection rate of 0.17 per patient year of follow-up (py) (95% CI 0.12–0.23). Patients with reinfections were all male and none of them self-described as PWID. The median age of these patients was 44 years (range 38–49). The main characteristics of reinfections and prescribed therapy are given in Table 2.

In 41 of 54 episodes of reinfection with available information on the use of recreational drugs, patients reported having chemsex (76%), especially with cocaine (49%), gamma-hydroxybutyrate/gamma-butyrolactone (GHB/GBL) (44%), methamphetamine (39%) and poppers (61%) (Table 3). The median number of sexual partners reported in the last month in 18 episodes of reinfections was 6.5 (range 3–34). Regarding sexual practices, in 48 cases (94%) of reinfection, patients acknowledged engaging in unprotected anal intercourse, 13 (43%) fisting, 33 (80%) sex partying and 6 (14%) slamming (Table 3). Second, third and fourth reinfections were detected in five, two and two patients, respectively, and the incidence of second infection was 0.09 per py (95% CI 0.03–0.15) and the incidence of third infection 0.11 per py (95% CI 0.04–0.17). All cases of second and third reinfections occurred in gbMSM who reported unprotected anal intercourse.
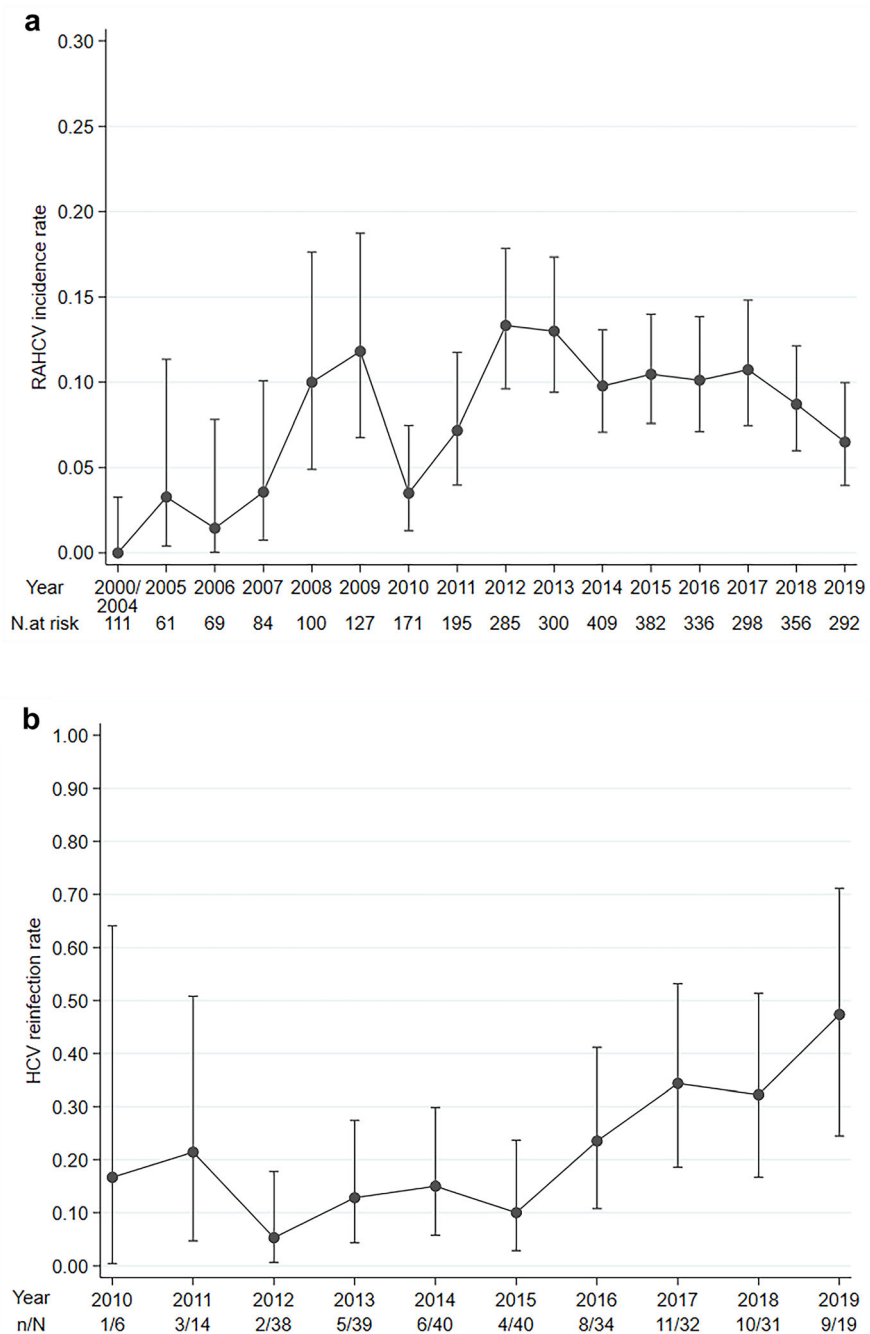
Fig. 1 a Incidence of newly acquired acute HCV infection in HIV-positive gbMSM. **b** HCV reinfection rates since 2010 in HIV-positive gbMSM. gbMSM gay, bisexual and other men who have sex with men; HCV hepatitis C virus; HIV human immunodeficiency virus

Before 2018, the yearly proportion of reinfection among the RAHCV infections ranged from 5% to 32%, while in 2019 it increased to 47% despite a lower number of RAHCV cases diagnosed in that year (Fig. 1b). Table 4 compares sexual behaviour risk factors between patients with new RAHCV and those with reinfection diagnosed in 2018 and 2019. A

Table 1 Characteristics of the 324 episodes recently acquired hepatitis C seen in 274 HIV-positive gbMSM

Characteristic	Value
Total no. of episodes per patient; $N = 274$	
1	233 (85)
2	35 (13)
3	4 (1)
4	1 (0.3)
5	1 (0.3)
HCV genotype; $N = 302$	
1	1 (0.3)
1a	113 (37)
1b	33 (11)
2	6 (2)
3	4 (1)
4	145 (48)
IL-28B haplotype; $N = 179$	
CC	78 (44)
CT	88 (49)
TT	13 (7)
CD4 count in cells/μL; $N = 310$	593 (452–764)
CD8 count in cells/μL; $N = 306$	824 (630–1126)
CD4/CD8 ratio; $N = 305$	0.72 (0.50–0.94)
HIV viral load in copies/mL; $N = 310$	
Detectable	63 (20)
Undetectable (< 50 to < 200)	247 (80)
AST/ALT (U/L); $N = 277$	77 (44–187)/170 (72–401)
Information on symptoms; $N = 125$	
Asymptomatic episodes	76 (61)
Reported symptoms in acute HCV infection*; $N = 49$	
Fatigue	39 (80)
Choluria	15 (31)
Nausea	14 (29)
Fever	6 (12)

Table 1 continued

Characteristic	Value
Jaundice	6 (12)
Abdominal pain	5 (10)
Anorexia	3 (6)
Vomiting	3 (6)
Therapy regimen in 275 treated episodes	
SOF/VEL	24 (9)
OBT/PTV/r ± DSV ± RBV	6 (2)
SOF/LDV	36 (13)
PEG/RBV	124 (45)
PEG/RBV/TEL	1 (0.4)
GLE/PIB	44 (16)
GZR/EBR	39 (14)
SOF/SMV	1 (0.4)
Months between diagnosis and starting therapy ($N = 244$) by year of RAHCV diagnosis	2.6 (1.8; 10.8)
2010–2015 ($N = 145$)	3.1 (1.9; 20.3)
2016–2017 ($N = 55$)	5.1 (2.5; 11.4)
2018–2019 ($N = 44$)	1.8 (1.3; 2.4)

Data are median (IQR), frequency (%). Data are presented without missing data
gbMSM gay, bisexual and other men who have sex with men; *HCV* hepatitis C virus; *HIV* human immunodeficiency virus; *DSV* dasabuvir, *EBR* elbasvir; *GLE* glecaprevir; *GZR* grazoprevir; *IQR* interquartile range; *LDV* ledipasvir; *OBT* ombitasvir; *PEG* pegylated interferon; *PIB* pibrentasvir; *PTV* paritaprevir; *RBV* ribavirin; *r* ritonavir; *SMV* simeprevir; *SOF* sofosbuvir; *TEL* telaprevir; *VEL* velpatasvir; *RAHCV* recently acquired hepatitis C
*We present most commonly (> 5%) reported symptoms of RAHCV episodes

higher proportion, although not significant, of gbMSM with reinfection reported high-risk sexual practices such as fisting (67%) and slamming (23%), compared to those with new

Table 2 Characteristics of the 60 reinfections diagnosed in 50 HIV-positive gbMSM

Characteristic	Value
Total no. of episodes per patient; $N = 50$	
1	45 (90)
2	3 (6)
4	1 (2)
5	1 (2)
HCV genotype; $N = 60$	
1a	26 (43)
1b	8 (13)
4	26 (43)
IL-28B haplotype; $N = 38$	
CC	17 (45)
CT	20 (53)
TT	1 (3)
CD4 count in cells/µL; $N = 60$	569 (452–702)
CD8 count in cells/µL; $N = 60$	874 (645–1061)
Ratio CD4/CD8; $N = 305$	0.66 (0.51–0.85)
HIV viral load in copies/mL; $N = 60$	
Detectable	4 (7)
Undetectable < 50	56 (93)
AST/ALT (U/L); $N = 56$	60 (35–104)/128 (49–242)
Information on symptoms; $N = 58$	
Asymptomatic episodes	45 (78)
Reported symptoms in reinfections*; $N = 13$	
Fatigue	11 (85)
Choluria	4 (31)
Nausea	3 (23)
Therapy regimen; $N = 55$	
SOF/VEL	8 (15)
SOF/LDV	9 (16)
PEG/RBV	15 (27)
GLE/PIB	12 (22)

Table 2 continued

Characteristic	Value
SOF/SMV	1 (2)
GZR/EBR	10 (18)
Months between diagnosis and starting therapy ($N = 54$) by year of reinfection diagnosis	2.5 (1.5; 6.7)
2010–2015 ($N = 19$)	3.6 (1.9; 20.9)
2016–2017 ($N = 17$)	3.2 (2.0; 11.7)
2018–2019 ($N = 18$)	1.5 (1.2; 2.1)

Data are median (IQR), frequency (%). Data are presented without missing data

EBR elbasvir; *gbMSM* gay, bisexual and other men who have sex with men; *GLE* glecaprevir; *GZR* grazoprevir; *HCV* hepatitis C virus; *HIV* human immunodeficiency virus; *IQR* interquartile range; *LDV* ledipasvir; *PEG* pegylated interferon; *PIB* pibrentasvir; *RBV* ribavirin; *SOF* sofosbuvir; *VEL* velpatasvir

*We present most commonly (> 10%) reported symptoms of HCV reinfection. Fever, vomiting, abdominal pain, acholia and anorexia were symptoms reported in 8% of episodes

infections (50% and 15%, respectively). Drugs used for chemsex did not vary significantly, but STIs were reported significantly more often by gbMSM with reinfection (10% vs 53%; $p = 0.0019$) (Table 4).

DISCUSSION

This study shows that the incidence of RAHCV infection among HIV-positive gbMSM in our cohort of PLWHIV in Barcelona was substantially high, especially from 2010 onwards, which is consistent with the increasing trends seen worldwide over the last decade [19–24].

However, the 40% decline in the cases of RAHCV infections in our cohort from 2017 to 2019 is remarkable and comparable to the 49%, 51% and 61% decrease in HCV incidence described in a real-life cohort in Switzerland

Table 3 Risk practices for HCV reinfections in 50 HIV-positive gbMSM

Category	All cases of HCV reinfections ($n = 60$)
No. of sex partners during last month; $N = 18$	
1	3 (17)
3–5	6 (33)
8–10	3 (17)
More than 10	6 (33)
Unprotected anal intercourse; $N = 51$	48 (94)
Sharing sex toys; $N = 34$	17 (50)
Fisting, $N = 30$	13 (43)
Drug use during sex; $N = 54$	41 (76)
Cocaine	20 (49)
GHB/GBL	18 (44)
Methamphetamine	16 (39)
Poppers	25 (61)
Ecstasy/MDMA	10 (24)
Erection-enhancing medication	12 (29)
Mephedrone	9 (22)
Speed	2 (5)
Sex partying; $N = 41$	33 (80)
Slamming drug intravenous; $N = 42$	6 (14)
STIs	36 (60)
Syphilis	31 (86)
Condyloma/HPV infection	4 (11)
Chlamydia and chlamydia/ LGV infection	10 (28)
Gonococcal infection	4 (11)
Proctitis unspecified	6 (17)
Urethritis unspecified	1 (3)

Table 3 continued

Category	All cases of HCV reinfections ($n = 60$)
Other STIs (molluscum, scabies, pediculosis)	1 (3)

Data are frequency (%). Data are presented without missing data

HCV hepatitis C virus; *HIV* human immunodeficiency virus; *IQR* interquartile range; *LGV* lymphogranuloma venereum; *MSM* men who have sex with men, *STIs* sexually transmitted infections

[10] and two real-life cohorts in the Netherlands [9, 25], respectively; but lower than that reported by Garvey et al. in UK [26], with a 78% decline for first HCV episode and 68% decline in overall HCV incidence. Similarly, HCV viraemic prevalence declined from 82% in 2014 to 8% in 2018 in the Australian CEASE cohort study [27]. All these findings are coincident with the introduction and generalization of DAA use, which supports the efficacy of generalized hepatitis C treatment as a prevention strategy for new HCV infections by reducing virus circulation within the gbMSM population. In relation to the time we take to treat patients from diagnosis, as can be observed, in general it is a short time, being the shortest time after 2017, when treatment in Spain with DDA was generalized, regardless of the degree of fibrosis or the time of diagnosis. Therefore, we do not think that reinfections or not new episodes may be due to untreated patients who remain viraemic.

In contrast to the decline of RAHCV, an increased rate of reinfection was observed at the end of the study period (2019), which reflects the heterogeneous risk of HCV infection and reinfection in this population [20]. The number of reinfections reported in our single centre study is high compared to those of recent large multicentre cohort studies in other regions of Europe. In our centre, 60 reinfections were detected in 244 gbMSM (24.5%). In the region of Madrid (Madrid CoRE cohort), reinfections

Table 4 Sexual behaviours for recently acquired HCV infections and for reinfections among gbMSM (period 2018–2019)

Category	New acute HCV ($n = 31$)	Reinfections ($n = 19$)	P value*
Sexualized drug users	16/24 (67)	13/17 (76)	0.729
Cocaine	7 (44)	5 (38)	0.774
Ketamine	3 (19)	3 (23)	1.000
GHB/GLB	9 (56)	5 (38)	0.340
Methamphetamine	10 (63)	7 (54)	0.638
Mephedrone	4 (25)	2 (15)	0.662
Speed	1 (6)	1 (8)	1.000
Ecstasy	2 (13)	1 (8)	1.000
MDMA	1 (6)	2 (15)	0.573
Poppers	6 (38)	7 (59)	0.379
Erection-enhancing medication	4 (25)	4 (31)	1.000
No. of sex partners	$N = 6$	$N = 4$	
2–3	2 (33)	0 (0)	
4–5	0 (0)	2 (50)	
7–30	3 (50)	0 (0)	
50	0 (0)	2 (50)	
60	1 (17)	0 (0)	
Unprotected anal intercourse	25/26 (96)	14/15 (93)	1.000
Use of sex toys	5/9 (56)	3/8 (38)	0.637
Fisting	5/10 (50)	4/6 (67)	0.633
Sex partying	13/15 (87)	7/10 (70)	0.358
Slamming drug intravenous	2/13 (15)	3/13 (23)	1.000
STIs	3/31 (10)	10/19 (53)	0.001

Table 4 continued

Category	New acute HCV ($n = 31$)	Reinfections ($n = 19$)	P value*
Syphilis	2 (67)	9 (90)	0.423
Condyloma/HPV infection	1 (33)	1 (10)	0.423
Chlamydia and chlamydia/LGV infection	1 (33)	3 (30)	0.528
Gonococcal infection	1 (33)	2 (20)	1.000
Proctitis unspecified	0 (0)	1 (10)	1.000
Urethritis unspecified	3 (100)	10 (100)	
Other STIs (molluscum, scabies, pediculosis)	3 (100)	10 (100)	

Data are n/N assessed (%), frequency (%). Data are presented without missing data

gbMSM gay, bisexual and other men who have sex with men; HCV hepatitis C virus; HIV human immunodeficiency virus; IQR interquartile range; GBL γ-butyrolactone; GHB γ-hydroxybutyric acid; LGV lymphogranuloma venereum; MDMA 3,4-methylenedioxymethamphetamine; STIs sexually transmitted infections

*Fisher's exact test or chi^2 test

were detected in 6.8% of gbMSM during the period 2014–2017 [11], while in Germany (GECCO cohort), 14.7% of MSM had become reinfected between 2014 and 2018 [12]. The MOSAIC cohort in the Netherlands showed the highest incidence rate in gbMSM among these multicentre cohorts (38.5 per 1000 py between 2000 and 2019 [95% CI 33.9–43.7] and declining to 11.4 per 1000 py in 2019) [9]. Similar findings were reported in the UK study by

Garvey et al. [26]. In contrast, the Australian CEASE cohort study only describes five reinfections in the period studied (2014–2017) [27]. One of the potential reasons for this low incidence is that 81% of the patients included in the CEASE cohort were PWID, showing an epidemiological scenario different from ours. The overall reinfection incidence after SVR of 0.17 per py in our study, which is approximately twice that of the Madrid-CoRe estimate (0.06 per py) [11] in the same setting of higher risk-taking behaviours, highlights the need for more effective application of risk-reducing strategies in our population.

The lack of PWID becoming reinfected in our cohort demonstrates the ongoing risk of repeated HCV transmission in gbMSM who engage in high-risk sexual practices and sexualized substance use [9, 11, 12, 18, 28]. The published information about specific risk factors associated with reinfection among MSM is scarce [12, 28]. Recently, the MOSAIC cohort [18] in a smaller group of patients in the Netherlands found an association between some sexual practices, such as receptive condomless anal intercourse, sex toy sharing, group sex, or at least 10 casual sex partners in the last 6 months, and reinfection. In our study almost all reinfections occurred during unprotected anal intercourse, chemsex, and sex toy sharing, as reported elsewhere [11, 18]. When we compare the reinfections and the new episodes that occurred in the last 2 years of our study, patients with reinfection presented a significantly higher proportion of STIs, and a higher non-significant trend of high prevalence of sexualized substance use, included slamming. The percentage of gbMSM practicing slam in our study (14%) was lower than that observed in Madrid-Core (33%) [11], reflecting the different epidemiological profiles of chemsex between studied cohorts and the dynamic and changing nature of the phenomenon.

Chemsex culture is spreading among gbMSM [15, 16] and had an impact on both new infections and reinfection episodes in our study. Chemsex practice is likely an indicator of the type of setting where sexual behaviours associated with HCV take place, and we found a high prevalence in our cohort in new RAHCV and

reinfection episodes. Unlike other studies, we asked specifically about the use of individual chemsex drugs and found a very common use of poppers, cocaine, methamphetamine and GHB/GBL. These results differ slightly from those observed in other countries and other Spanish regions, where mephedrone was one of the main sexualized drugs among MSM [29, 30], and demonstrate the dynamic nature and cultural variation of chemsex phenomenon, a fact that has to be taken into account when designing specific prevention strategies [31]. The social and personal factors involved in chemsex are as diverse as the barriers to reduce HCV-related sexual risk behaviour in this population, including social pressure, and HCV-HIV and drug consumption stigma [32]. This points to the importance of thorough characterization of risk factors in patients attending our clinics to offer effective prevention interventions. Chemsex and high-risk sexual practices are likely the current barriers to HCV elimination in our setting. The decline in prevalence of chemsex over time among MSM observed in the AURAH2 study, which has been attributed to the participation of specialized centres for chemsex support [33], is a reflection on the effectiveness of tailored prevention strategies.

Our population does not appear to be at elevated risk of subsequent reinfection, with a second reinfection incidence that is twofold lower than the first.

Another interesting scenario that we will have to assess for HCV microelimination in our setting will be in MSM users of HIV pre-exposure prophylaxis (PrEP). The approval of the use of PrEP by the Spanish national health system is effective from November 2019. Currently in our hospital we have more than 250 users in follow-up. We will have to closely monitor what happens with this group, especially with PrEP users who present a risk profile for hepatitis C similar to the one described in our work.

The strengths of this study include a large real-life cohort in a single centre, thus minimizing variations in clinical practice, and the information provided on drug use and risk behaviours of a reinfection sample size that is larger than in other published studies. The information generated can be extrapolated and

used in other medical centres of European cities with an important gay community similar to that of our centre. The study has some limitations, including its descriptive and retrospective nature and the fact that the risk of determinants for HCV infection was not analysed. Therefore, conclusions on risk factors in patients with a single episode of RAHCV versus those who became reinfected over the studied period cannot be drawn; being aware of this will aid us in designing a prospective study addressing the weakness of this analysis. Nonetheless, this study defines factors associated with a higher risk of HCV infection and reinfection to anticipate new RAHCV episodes. The magnitude of recreational drug use during sex and sexual risk-taking behaviours in gbMSM, as well as the increased prevalence of STIs, must be kept in mind when designing public harm-reduction and prevention approaches in this population. Moreover, screening strategies for STIs and frequent testing for HCV-RNA in high-risk groups should be promoted to ensure diagnosis and early treatment.

In conclusion, despite the decline in the incidence of HCV episodes observed in our cohort, HCV reinfection has increased in recent years in gbMSM living with HIV, indicating the high risk for HCV transmission in this population. The high frequency of chemsex use and other sexual risk-taking behaviours demand tailored public health harm-reduction interventions.

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