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ORIGINAL ARTICLE

The 'Viennese epidemic' of acute HCV in the era of direct-acting antivirals

David Chromy[1,2,3] | David J. M. Bauer[1,2] | Benedikt Simbrunner[1,2] | Matthias Jachs[1,2] | Lukas Hartl[1,2] | Philipp Schwabl[1,2] | Caroline Schwarz[1,2,4] | Armin Rieger[2,3] | Katharina Grabmeier-Pfistershammer[2,5] | Michael Trauner[1,2] | Peter Ferenci[1] | Mattias Mandorfer[1,2] | Michael Gschwantler[2,4] | Thomas Reiberger[1,2]

[1]Division of Gastroenterology and Hepatology, Department of Internal Medicine III, Medical University of Vienna, Vienna, Austria

[2]Vienna HIV & Liver Study Group, Vienna, Austria

[3]Department of Dermatology, Medical University of Vienna, Vienna, Austria

[4]Department of Internal Medicine IV, Wilhelminenspital, Wiener Gesundheitsverbund (WiGeV) der Stadt Wien, Vienna, Austria

[5]Center for Pathophysiology, Infectiology and Immunology, Institute of Immunology, Medical University Vienna, Vienna, Austria

Correspondence
Thomas Reiberger, Division of Gastroenterology and Hepatology, Department of Internal Medicine III, Medical University of Vienna, Waehringer Guertel 18-20, 1090 Vienna, Austria.
Email: thomas.reiberger@meduniwien.ac.at

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Abstract

The recently reported epidemic of acute hepatitis C virus (HCV) infections —observed predominantly among men who have sex with men (MSM)—may now decline due to wide availability of direct-acting antivirals (DAAs). This study aimed to investigate the current trends of acute hepatitis C in Vienna. Patients presenting with acute hepatitis C between 01/2007 and12/2020 at the Vienna General Hospital were retrospectively enrolled and followed after virologic clearance/eradication. The introduction of unrestricted DAA access after 09/17 defined the 'DAA era', as compared to the 'pre-DAA era' prior to 09/17. We identified 134 acute hepatitis C cases in 119 patients with a mean age of 39 ± 9 years at inclusion. The majority of patients were male (92%), HIV-positive (88%) and MSM (85%). In the DAA era, a history of prior chronic HCV infection at inclusion was found in 24% (11/46) compared to 7% (5/73) in the pre-DAA era ($p = .012$). The annual rate of acute hepatitis C cases increased in the DAA era (17.11 per year) compared to the pre-DAA era (7.76 per year). The DAA era included an AHC-genotype-2 cluster and more HIV-negative acute hepatitis C cases (0% (0/73) vs. 30% (14/46), $p < .001$). Patients were followed after spontaneous clearance or sustained virologic treatment response (SVR) for a total of 251.88 patient-years (median 1.39 years per patient). In the DAA era, we recorded 15 acute hepatitis C-reinfections — corresponding to an incidence rate of 5.96 (95% CI: 3.57–9.66) reinfections per 100-patient-years. We continue to observe a high incidence of acute hepatitis C in Vienna in the DAA era—primarily among HIV-positive MSM, but increasingly also in HIV-negative MSM.

KEYWORDS
hepatitis C virus, human immunodeficiency virus, men who have sex with men, PrEP, sexualized drug use

Abbreviations: AHC, acute HCV infection; AIDS, acquired immunodeficiency syndrome; ALT, alanine transaminase; ART, Antiretroviral therapy; CI, confidence interval; COVID-19, coronavirus disease; DAA, direct-acting antivirals; GT, genotype; HCV, hepatitis C virus; HIV+, HIV positive; HIV, human immunodeficiency virus; IFN, interferon; IQR, interquartile range; MSM, men who have sex with men; PrEP, pre-exposure prophylaxis for HIV; PWID, people who inject drugs; PY, patient-years; Q3, third quarter; Q4, fourth quarter; RNA, ribonucleic acid; sCL, spontaneous clearance; STI, sexually transmitted infection; SVR, sustained virologic response; ULN, upper limit of normal; WHO, world health organization.

1 | INTRODUCTION

Even after the introduction of direct-acting antivirals (DAA) as modern treatment for hepatitis C virus (HCV) infection, several western countries still report high incidence of both de-novo and re-acquired acute HCV (AHC) infections.[1,2] An ongoing epidemic of AHC infections among HIV-positive (HIV+) men who have sex with men (MSM) starting in the early 2000s had been described before[3,4] and while the global scale-up of DAA treatment would give reason to expect declining numbers, several recently published studies indicate a persistent and florid HCV outbreak.[5,6] Nevertheless, other cohorts reported already of a decline in HCV incidence since DAAs were established.[7,8]

For MSM—the affected key population—high-risk sexual behaviour, HIV status, presence of sexually transmitted infections (STI) and sexualized drug use ('chemsex') are well-described risk factors for the acquisition of HCV.[9–11] Additionally, several case series have reported a rising number of AHC infections among HIV-negative MSM using pre-exposure prophylaxis for HIV (PrEP).[12,13] Phylogenetic analyses of HCV variants of HIV+ and HIV-negative MSM suggest HCV transmission among serodiscordant partners and thus put HIV-negative MSM on PrEP at particular risk.[14]

The world health organization (WHO) has set a goal to reduce the incidence of viral hepatitis by 90% until 2030.[15] Modelling data suggest that multiple actions are needed to achieve this ambitious goal for HCV elimination, including treatment scale-up, early treatment initiation, harm reduction and offensive screening initiatives.[16] A recent HIV+ MSM community study conducted in Berlin concluded that a combination of early DAA uptake and behavioural interventions are required to reduce the numbers of HCV incidence.[17] One recommended approach is 'micro-elimination', which considers local/specific needs and limitations, and thus, allows for specifically tailored HCV elimination projects for different regions/patient populations.[18] However, the successful design/conduct of 'micro-elimination' projects aiming at reducing the burden of the ongoing AHC epidemic requires a good understanding of the local epidemiology.

In Austria, DAAs became first available in January 2015 but due to the high initial costs, treatment was only reimbursed for certain patient with higher fibrosis stages, and thus, fibrosis screening strategies were needed to identify eligible patients.[19] While some scale-up of HCV treatment was achieved in Austria,[20,21] the concept of 'treatment as prevention' could only be considered, once DAAs were reimbursed for all HCV-infected individual, starting from September 2017. In order to inform future Austrian HCV elimination strategies, we aimed to investigate the patient characteristics and dynamics in the incidence of AHC infection before and after restricted DAA access in Vienna, and also assessed the incidence rate of HCV reinfection.

2 | PATIENTS AND METHODS

2.1 | Study design and population

All patients at the Vienna General Hospital with suspected AHC infection between Q3/2007 and Q4/2020 were screened for this retrospective study. Individuals with confirmed AHC infection were finally included. The clinical course of the AHC infection was assessed and categorized as (i) spontaneous clearance, (ii) progression towards chronic HCV infection, (iii) loss to follow-up and (iv) treatment initiation (including treatment outcome). All patients achieving HCV cure—either by spontaneous clearance or by treatment-induced sustained virologic response (SVR)—were followed, and cases of HCV reinfection were documented.

2.2 | Definitions and outcome

While we refer to the term acute HCV (AHC) infection in the present study, the definition for AHC is derived from the criteria for recently acquired HCV infection defined by the European AIDS Treatment Network (NEAT-ID).[22] The first 6 months of HCV infection were defined as acute infection, while the first 12 months were defined as early infection and (any of) the following criteria was used for diagnosis: (i) a positive anti-HCV-antibody test in the presence or absence of a positive HCV-RNA test and a documented negative anti-HCV-antibody test in the previous 12 months; or (ii) positive HCV-RNA and a documented negative HCV-RNA and negative anti-HCV-antibody test in the previous 12 months. In case of missing historical data of the past year, alternative diagnostic criteria for acute HCV infection were applied: A positive HCV-RNA test regardless of anti-HCV-antibody test and an acute rise in alanine transaminase (ALT) greater than 3 times the upper limits of normal (ULN) with documented normal ALT within 12 months, an association with ongoing risk behaviour and exclusion of other causes of acute hepatitis.[22]

Acute reinfection with HCV was diagnosed when all of the following criteria applied: (i) previously documented spontaneous clearance or SVR and (ii) presence of acute HCV infection as defined by the criteria above and detection of a different HCV-genotype (HCV-GT) as compared to the previous HCV infection.

Spontaneous clearance of HCV infection was defined as two negative HCV-RNA (with 12 weeks in-between) following the diagnosis of acute HCV (re)infection without therapeutic interventions. If treatment was initiated, SVR was defined as one or more negative HCV-RNA tests 12 weeks after completion of therapy.

The date of achieving either spontaneous clearance or SVR was considered as the start of follow-up. Patients had follow-up HCV-RNA tests every 3–6 months. Individuals without a visit at the clinic for more than 12 months were considered 'lost to follow-up'.

The introduction of nationwide unrestricted DAA access after 09/2017 defined the 'DAA-era', as compared to the 'pre-DAA-era' prior to 09/2017. For some sub-analyses, the 'pre-DAA-era' was also separated into the 'interferon (IFN)-era' from 01/2007 to 12/2014 and 'restricted DAA access' from 01/2015 to 08/2017 in which DAAs were only reimbursed for patients with severe liver disease (i.e., fibrosis stages ≥F2).

2.3 | HCV therapy

Recommendations for the treatment of AHC/chronic hepatitis C at respective time at AHC onset guided patient management and

treatment initiation. Furthermore, the choice of DAA and the respective treatment regimen had to comply with local reimbursement restrictions.[23] A decrease of 2 $\log_{10}$ of HCV-RNA within 4 weeks after onset of AHC infection without treatment was considered indicative for spontaneous clearance and treatment initiation was deferred.[24]

2.4 | Parameters

All epidemiological, demographical and clinical parameters and patient characteristics were collected from patients' medical record. Commercially available anti-HCV-antibody, HCV-RNA and HCV-GT assays were used.

2.5 | Statistical analysis

Statistical analyses were performed using GraphPad Prism 8 (GraphPad Software) and IBM SPSS Statistics 25 (IBM). Gaussian normal distribution of continuous variables was tested by plotting the data as histograms. Continuous parameters are displayed as mean ± SD, or in case of non-parametric distribution, as median with quartiles (range from the 25th to the 75th percentile). Categorical parameters are presented as number and proportion of patients. Group comparisons of continuous variables were performed with Students' *t*-test or Wilcoxon–Mann–Whitney U-test. Categorical variables were compared with chi-squared test or Fisher's exact test, when applicable. To calculate the incidence rate of reinfections during follow-up and the respective 95% confidence interval (95% CI), the person-time method was used. Unrestricted DAA access in Austria began in September 2017; this time point was used for stratification. The level of significance for statistical analyses was set at 0.05.

2.6 | Ethics

This study was conducted in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Declaration of Helsinki and its later amendments and approved by the local ethics committee of the Medical University of Vienna (MUW-EK 1968/2018). The need for an informed consent was waived by the ethics committee of the Medical University of Vienna due to the retrospective design.

3 | RESULTS

3.1 | Observed cases of acute HCV infection

One hundred thirty-four patients presented at our outpatient clinic with suspected AHC infection. Twelve per cent (16/133) had a history of chronic HCV infection. Of all 133 patients, acute and early HCV infection were confirmed in 81% (108/133) and 8% (11/133), respectively, while 11% (14/133) did not meet the criteria (Figure 1). Among the 119 diagnosed individuals, one patient was lost to follow-up after diagnosis while we observed spontaneous clearance in 10% (12/118), leaving 90% (106/118) for potential treatment initiation. Of those, 5% (5/106) required re-therapy following interferon-based treatment failure and four more patients were lost to follow-up during therapy. One hundred fourteen individuals achieved spontaneous or treatment-induced virologic clearance and were followed for a total of 251.88 patient-years (PY). During follow-up, we observed 15 acute HCV reinfections in 9% (13/114) of patients whereas one individual presented only with chronic HCV infection. The majority of reinfections during follow-up occurred in MSM (77%, 10/13), including the two individuals with a documented second reinfection.

Throughout the observational period from Q3/2007 to Q4/2020, we observed 119 individuals with 134 cases of acute HCV infection (Figure 2), which translates to a number of 10.11 incident cases per year. When analysing the cases (including reinfections during follow-up) by the different time periods of HCV treatment availability, the yearly number of cases rose from 5.38/year in the IFN-era, to 14.25/year during restricted DAA access and to 17.11/year during the DAA era (Table 1). The overall follow-up time was 251.88 years within which we observed 15 cases of acute HCV reinfection resulting in an incidence rate of 5.96 per 100PY (95% CI 3.57–9.66).

3.2 | Patient characteristics

The mean age at presentation of individuals with confirmed AHC was 38.9 ± 8.69 years, the majority (92%, 110/119) was male, the suspected route of HCV transmission was MSM in 85% (99/117) and 88% (105/119) were HIV+ (Table 2). The median HCV viral load at presentation was 5.78 log IU/ml (IQR 2.93), the median peak ALT was 361 U/L (IQR 681), and 13% (16/119) had a history of HCV according to their previous records. HCV-GT could not be determined due to low HCV viral load at initial presentation in 5% (6/113). Among the 100 available HCV-GT results, the most prevalent was GT-1a with 70% (79/113).

3.3 | Characteristics of AHC patients with spontaneous clearance

(Table 3) Among patients with spontaneous clearance, the proportion of people who inject drugs (PWID; vs. MSM as suspected route of transmission) was higher than in AHC patients with persisting HCV viraemia and/or who required antiviral therapy (42% vs. 12%; $p = .024$). As expected, the HCV-RNA levels at initial presentation were significantly lower in AHC patients achieving spontaneous clearance (1.46 log IU/ml (IQR 1.04) vs. 6.02 log IU/ml (IQR 2.53); $p < .001$). Interestingly, 42% (5/12) of individuals who experienced spontaneous clearance were reinfected during follow-up, and of those, 60% (3/5) again showed spontaneous HCV clearance. Both HIV status and sufficient HIV-RNA suppression below <50 copies/

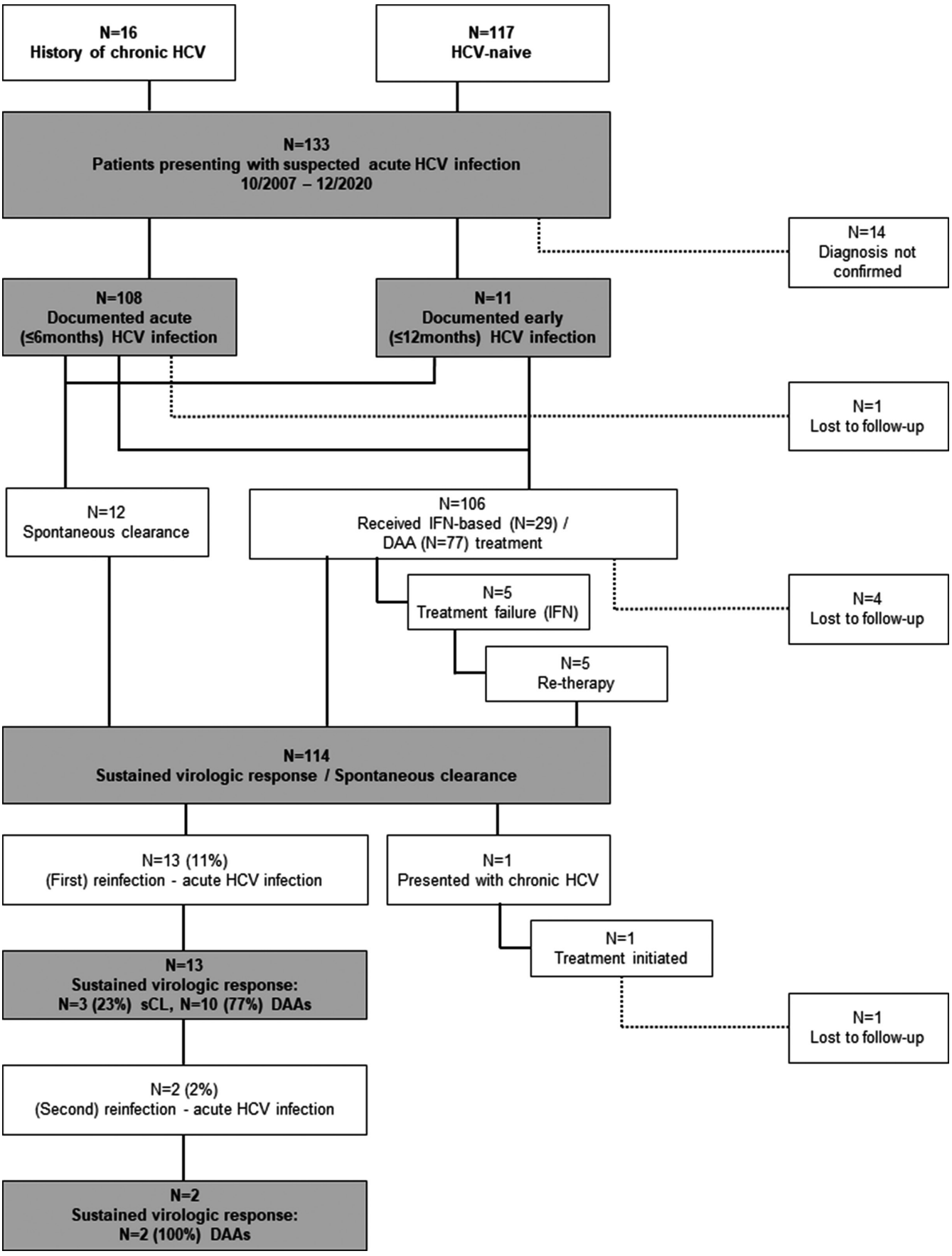

FIGURE 1 Patient consort diagram. DAA, direct-acting antivirals; HCV, hepatitis C virus; IFN, interferon; sCL, spontaneous clearance

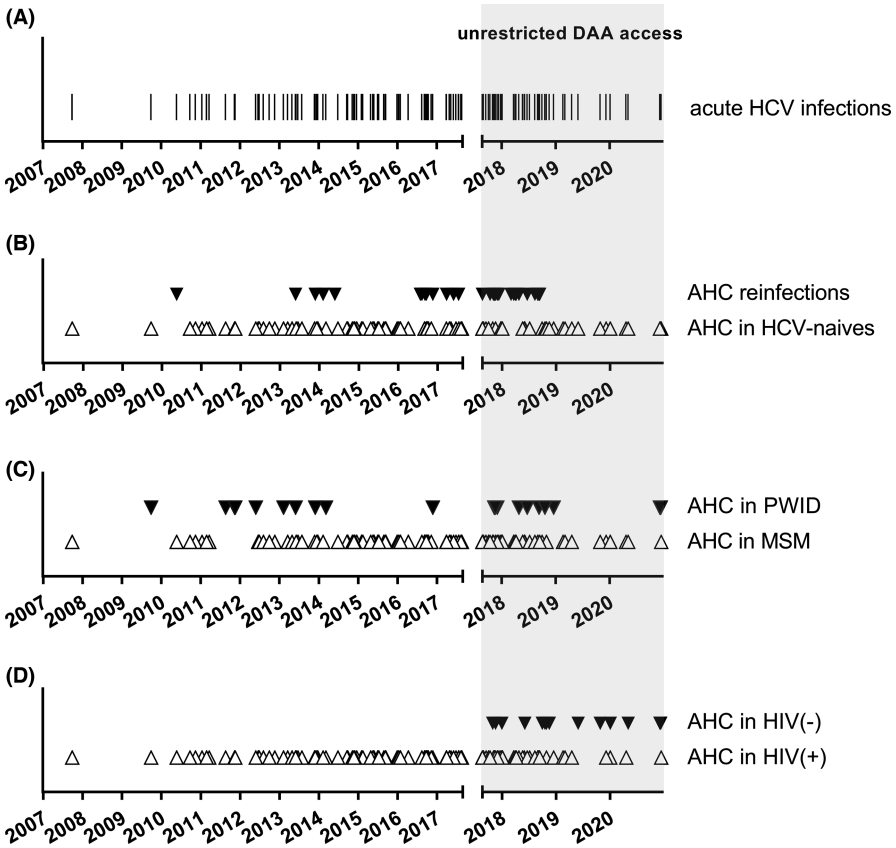

FIGURE 2 Overall incident acute HCV infections during the observational period (A) and incident acute HCV infections stratified by status of previous HCV infections (B), by mode of transmission (C) and by HIV status (D). In panel (A) each line denotes a single case of acute HCV infection. In panel (B–D) each black or white triangle denotes a single case of acute HCV infection of the respective category. AHC, acute HCV infection; HCV, hepatitis C virus; MSM, men who have sex with men; PWID, people who inject drugs

mL had no statistically significant impact on the rate of spontaneous HCV clearance. Nevertheless, all HIV+ patients experiencing spontaneous clearance were on antiretroviral therapy (ART) and had HIV-RNA levels below <50 copies/ml.

3.4 | The DAA era

Since September 2017, the Austrian healthcare providers reimbursed DAAs without restrictions. Seventy-seven cases of acute HCV infection were seen in the period before, whereas 57 cases emerged afterwards in the DAA era. Notably, the 57 cases of AHC did occur across the time periods as followed: 2017 (the remaining 4 months) $N = 17$, 2018 $N = 26$, 2019 $N = 7$ and 2020 $N = 7$. Significantly more patients presenting in the DAA era had a history of HCV (24% (11/46) vs. 7% (5/73) in the pre-DAA era; $p = .012$), and we observed an increasing number of HCV-GT2 infections (16% (7/44) after vs. 0% (0/69) before; $p < .001$).

Interestingly, cases of AHC infection among HIV-negative individuals were exclusively seen in the DAA era: While in the pre-DAA era, all AHC cases (100%, 73/73) were HIV-coinfected, the rate of AHC-HIV coinfection dropped to 70% (32/46; $p < .001$) once DAAs were readily reimbursable. Nine of the 14 cases among HIV-negative patients were MSM and 56% (5/9) were using PrEP. Of note, the 'cluster' of AHC infections with GT2 in the DAA era affected both HIV+ (71%, 5/7) and HIV-negative individuals (29%, 2/7).

4 | DISCUSSION

We observed a consistent rise in the numbers of AHC infections - mostly in HIV+ MSM - in Vienna throughout the 13 years (2007–2020) included the study period, with a further aggravation after DAAs became accessible and HIV-negative MSM being increasingly affected. Importantly, we also found a high HCV reinfection rate of 11% during a median follow-up of 1.39 years after HCV clearance/SVR in the DAA era. These findings clearly indicate that Vienna was and remains affected by the ongoing epidemic of AHC infections among HIV+ and HIV-negative MSM.

In 2019, Todesco et al.[25] reported a recent outbreak of AHC infections affecting 85 HIV+ MSM in Paris with a quarter of all infections being reinfections. The phylogenetic analysis performed in this study proved a strong clustering of certain HCV strains within the affected population. Han et al.[26] published 48 cases of AHC infections among MSM in Thailand that were phylogenetically investigated, and 92% of AHC cases were represented in only two different clusters. These results suggested ongoing risk behaviour and recent onward transmission within this Thai cohort of individuals at risk for HCV acquisition. While phylogenetic data are not available in our study, the observed HCV-GT 2 cluster, a HCV-GT that was restricted to the more recent AHC cases during the DAA era, strongly suggests a linkage between these cases.

However, broad DAA access has a strong potential to eliminate HCV in certain populations: Recent surveillance data from Australia indicate a decline of 78% in HCV incidence in 2019 as compared to

TABLE 1 Incident HCV infections throughout different treatment eras

		Infections per year including reinfections during follow-up		
Overall				
31-Dec-20 – 1-Oct-07		10.11		
Cases of acute HCV	*N* = 134			
DAA era				
31-Dec-20 – 1-Sep-17		17.11		
Cases of acute HCV	*N* = 57			
2017[a]	*N* = 17			
2018	*N* = 26	26.00		
2019	*N* = 7	7.00		
2020	*N* = 7	7.00		
Restricted DAA access				
1-Sep-17 – 1-Jan-15		14.25		
Cases of acute HCV	*N* = 38			
IFN-era				
1-Jan-15 –1-Oct-07		5.38		
Cases of acute HCV	*N* = 39			
			Reinfections per 100-patient-years	95%-Confidence interval
Overall follow-up after SVR				
Median follow-up per patient	1.39 years			
Patient-years	251.88 years		5.96	3.57–9.66
Cases of AHC reinfection	*N* = 15			

Abbreviations: AHC, acute HCV infection; DAA, direct-acting antivirals; HCV, hepatitis C virus; IFN, Interferon; SVR, sustained virologic response.
[a]Includes only Sep–Dec.

2015.[8] This analysis included more than twenty-thousand gay and bisexual men and attributed the observed decrease in HCV infections primarily to increased DAA availability.[8] Data of the Swiss HIV Cohort Study also reported a significant decline in HCV incidence in 2019 among MSM following a systematic screening and treatment programme executed from 2015 to 2017.[27] A cross-sectional study from Spain comprising data from 2016 to 2018 demonstrated a lower prevalence of HCV, after DAAs were introduced.[28]

However, in contrast to chronic HCV infections, results on dynamics of AHC infection are scarce: Garvey et al.[7] published incidence rates from London and Brighton over the period 2013 to 2018. In HIV+ MSM, a significant reduction in AHC was observed after 2017, which was attributed to the drastically reduced time from diagnosis to treatment initiation (29.8 months in 2013 down to 2.7 months in 2018) by the authors. Cumulating real-world data show that early access to DAA treatment in certain HCV risk groups is an effective measure to prevent HCV transmission.[16,17] Furthermore, modelling analyses have demonstrated that early treatment of AHC is more cost efficient than waiting for chronification of HCV infection.[29] Consequently, current HCV treatment guidelines recommend immediate treatment initiation once AHC diagnosis is established following the concept of 'treatment as prevention'.[30,31]

While our study did not aim to investigate the efficacy of different treatment regimens, we have previously published an excellent SVR rate of 100% in 38 AHC patients receiving DAAs.[23] This might have also contributed to the decline of newly diagnosed AHC infections in 2019–2020, with only 7.0/year after a peak of AHC infections observed in 2017–2018 (17.11/year). However, this observation should not be overemphasized, since the concomitant COVID-19 pandemic may have negatively impacted the local cascade of care in 2019–2020, which may have led to reduced referrals.[32]

Importantly, we observed 15 HCV reinfections during follow-up corresponding to a reinfection rate of almost 6 per 100-PY. A recent report from the MOSAIC study group in the Netherlands on HIV+ MSM reported even higher reinfection rates of 11.5 per 100-PY,[33] whereas the German NEAT and GECCO studies reported lower rates among HIV+ and HIV- MSM and PWIDs of 1.89 reinfections per 100-PY.[6] The authors of both studies conclude that ongoing risk behaviour was strongly associated with reinfection. In our study, we had very limited information on specific risk, since only information on the suspected route of HCV transmission was available. Nevertheless, previous studies have demonstrated that the vast majority of Austrian HCV-infected MSM engaged in sexualized drug use and condomless anal intercourse[9]—two well-established high-risk practices for HCV acquisition.[34]

TABLE 2 Patient characteristics

	All patients (*N* = 119)	pre-DAA era (*N* = 73)	DAA era (*N* = 46)	*p*-Value
Epidemiological characteristics				
Age (years)	38.9 ± 8.69	39.5 ± 8.43	37.9 ± 9.10	.338
Male (%, *n*/all)	92% (110/119)	96% (70/73)	87% (40/46)	.087
Primary suspected transmission risk[a]				
MSM (%, *n*/all)	85% (99/117)	89% (65/73)	77% (34/44)	.071
PWID (%, *n*/all)	15% (18/117)	11% (8/73)	23% (10/44)	
HIV infection parameters				
HIV-positive (%, *n*/all)	88% (105/119)	100% (73/73)	70% (32/46)	<.001
Median time since HIV diagnosis (IQR)	6.59 (9.98)	6.76 (9.68)	5.15 (12.5)	.951
Receiving ART (%, *n*/all)[b]	97% (98/101)	97% (67/69)	97% (31/32)	1
HIV-RNA < 50 copies ml^{-1} (%, *n*/all)	86% (74/86)	84% (48/57)	90% (26/29)	.743
CD4+ T-lymphocyte count (cells μl^{-1})	669 ± 256	669 ± 254	669 ± 265	.993
HCV infection parameters				
History of chronic HCV (%, n/all)	13% (16/119)	7% (5/73)	24% (11/46)	.012
HCV-RNA (log IU ml^{-1})	5.78 (2.93)	6.06 (2.27)	4.96 (3.30)	.050
HCV-genotype (%, *n*/all)				
1a	70% (79/113)	75% (52/69)	61% (27/44)	<.001
1b	8% (9/113)	12% (8/69)	2% (1/44)	
2	6% (7/113)	0% (0/69)	16% (7/44)	
3	6% (7/113)	1% (1/69)	14% (6/44)	
4	9% (10/113)	10% (7/69)	7% (3/44)	
6	1% (1/113)	1% (1/69)	0% (0/44)	
Peak ALT ($U L^{-1}$)	361 (681)	405 (651)	292 (706)	.168
Peak Bilirubin (mg/dl)	0.56 (0.44)	0.61 (0.48)	0.48 (0.30)	.035
Spontaneous clearance	10% (12/119)	14% (10/73)	4% (2/46)	.125

Abbreviations: ALT, alanine transaminase; ART, antiretroviral therapy; DAA, direct-acting antivirals; HCV, hepatitis C virus; IQR, interquartile range; MSM, men who have sex with men; PWID, people who inject drugs.

[a]Two individuals infected by needle-stick injury are not included.

[b]Four HIV-positive individuals had no information on ART-use available.

Another typical marker for increased risk for HCV transmission is positive HIV status.[35] However, increasing rollout of PrEP in the recent years may has shifted this paradigm. As PrEP enables sufficient protection against HIV infection,[36] individuals engaging in high-risk sex practices likely maintain their HIV-negative status and—in some cases—even over-compensate by scaling their risk behaviour further up.[13] A recent meta-analysis by Ong et al.[37] on STIs among PrEP-users reported not only extremely high rates of chlamydia and gonorrhoea, but also an HCV prevalence of 2% at PrEP-initiation. In our data, we also noted an increase in acute HCV infections among HIV-negative individuals. Fourteen AHC cases in HIV-negative occurred exclusively in the DAA era, and 56% of the affected MSM were using PrEP. In 2021, PrEP is still not fully covered by the healthcare providers in Austria, and thus, PrEP rollout is strongly hampered in our country.[38] Nevertheless, recent HIV-negative cases may reflect the internationally observed shift of the population at risk from HIV+ MSM to HIV-negative MSM on PrEP.[11] Fortunately, regular STI screening—including HCV testing—is mandated during PrEP use; hence, PrEP-care might also allow sufficient and regular HCV screening in MSM practicing high-risk behaviour.[39]

A major strength of our study is the long observational period spanning over more than a decade and ranging back to the first reports on the acute HCV pandemic. This is also the first report providing details on the dynamics of incident acute HCV infections in Vienna. In addition, we also provide important information on the incidence rate of HCV reinfections. Our findings will allow to design specific screening and treatments programmes (i.e., micro-elimination) targeting the high-risk group of HIV+ and HIV-negative MSM engaging in high-risk HCV transmission behaviour. Importantly, a first MSM-targeted HCV screening programme has already been conducted in Vienna.[40]

However, our study also has limitations: First, the retrospective design is likely prone to bias. As a tertiary care centre, the numbers of incident AHC at our clinic are to some extent dependent on a referral structure that may have changed throughout the years. Second, the presented study includes only data from a single centre. Third, our study lacks phylogenetic analyses of HCV, which could

TABLE 3 Characteristics of patients with spontaneous HCV clearance

	All patients (*N* = 119)	Spontaneous clearance (*N* = 12)	No spontaneous clearance (*N* = 107)	*p*-Value
Epidemiological characteristics				
Age (years)	38.9 ± 8.69	35.9 ± 7.61	39.2 ± 8.77	.206
Male (%, *n*/all)	92% (110/119)	92% (11/12)	93% (99/107)	1
Transmission[a]				
MSM (%, *n*/all)	85% (99/117)	58% (7/12)	88% (92/105)	.024
PWID (%, *n*/all)	15% (18/117)	42% (5/12)	12% (13/105)	
HIV infection parameters				
HIV status (%, *n*/all)	88% (105/119)	100% (12/12)	87% (93/107)	.356
Median time since HIV diagnosis (IQR)	6.59 (9.98)	5.90 (13.5)	6.73 (10.1)	.978
Receiving ART (%, *n*/all)[b]	97% (98/101)	100% (9/9)	97% (89/92)	1
HIV-RNA <50 copies ml^{-1} (%, *n*/all)	86% (74/86)	100% (5/5)	85% (69/81)	1
CD4+ T-lymphocyte count (cells μl^{-1})	669 ± 564	631 ± 170	670 ± 259	.833
HCV infection parameters				
Prior episode of HCV (%, *n*/all)	13% (16/119)	25% (3/12)	12% (13/107)	.204
HCV-RNA (log IU ml^{-1})	5.78 (2.93)	1.46 (1.04)	6.02 (2.53)	<.001
Peak ALT (U L^{-1})	361 (681)	422 (1 109)	351 (596)	.805
Bilirubin (mg dl^{-1})	0.56 (0.44)	0.59 (0.99)	0.56 (0.44)	.889

Abbreviations: ALT, alanine transaminase; ART, antiretroviral therapy; HCV, hepatitis C virus; IDU, intravenous drug use; IQR, interquartile range; MSM, men who have sex with men; PWID, people who inject drugs.

[a]Two individuals infected by needle-stick injury are not included.

[b]Four HIV-positive individuals had no information on ART-use available.

be used to further define reinfections and detect spread of HCV through clusters within a risk population.

In conclusion, we observed an increasing number of AHC infections in Vienna that peaked in the DAA era and predominantly affected HIV+ and but also HIV-negative MSM. The rate of reinfection was also high and similar to recent observations from other European cohorts. Thus, consistent screening of the populations at risk for AHC infection is required to enable early 'treatment as prevention'.

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CONFLICT OF INTEREST

DC served as a speaker and/or advisory board member for AbbVie, Gilead, ViiV Healthcare and MSD, and received travel support from AbbVie, MSD, ViiV Healthcare and Gilead. **DB** has received speaker fees from AbbVie and Siemens, travel support from AbbVie and Gilead, and grant support from Philips, Gilead and Siemens. **BS** received travel support from AbbVie and Gilead. **MJ** served as a speaker for Gilead. **LH** nothing to disclose. **PS** received consulting fees from PharmaIN. **CS** received travel support from Gilead, AbbVie and Gebro, and speaking honoraria from AbbVie and Gilead. **AR** served as a speaker and/or advisory board member for Gilead Sciences, ViiV Healthcare and MSD. **KGP** served as a speaker and/or advisory board member for Gilead Sciences, ViiV Healthcare and MSD. **MT** has served as speaker for Falk Foundation, Gilead, Intercept and MSD; he has advised for Albireo, BiomX, Boehringer-Ingelheim, Falk Pharma GmbH, Genfit, Gilead, Intercept, Jannsen, MSD, Novartis, Phenex, Regulus and Shire. He further received travel grants from Abbvie, Falk, Gilead and Intercept and research grants from Albireo, Alnylam, Cymabay, Falk, Gilead, Intercept, MSD Takeda and UltraGenyx. He is also co-inventor of patents on the medical use of NorUDCA filed by the Medical Universities of Graz and Vienna. **PF** served as a speaker and/or advisory board member for Gilead, AbbVie and Vivaraxx AG and received grant support from Gilead. **MM** served as a speaker and/or consultant and/or advisory board member for AbbVie, Bristol-Myers Squibb, Gilead, Collective Acumen, and W. L. Gore & Associates and received travel support from AbbVie, Bristol-Myers Squibb and Gilead. **MG** received grant support from Abbvie, Gilead and MSD; speaking honoraria from Abbvie, Gilead, Janssen, Roche, Intercept and MSD; consulting/advisory board fees from Abbvie, Gilead, Janssen, Roche, Intercept, Norgine, AstraZeneca, Falk, Shionogi and MSD; and travel support from Abbvie and Gilead. **TR** received grant support from Abbvie, Boehringer-Ingelheim, Gilead, Gore, Intercept, MSD, Myr Pharmaceuticals, Philips Healthcare, Pliant and Siemens; speaking honoraria from Abbvie, Gilead, Gore, Intercept, Roche, MSD; consulting/advisory board fee from Abbvie, Bayer, Boehringer-Ingelheim, Gilead, Intercept, MSD, Siemens; and travel support from Abbvie, Boehringer-Ingelheim, Gilead and Roche.

AUTHOR CONTRIBUTIONS

DC, DB, MM, MG and TR involved in study concept and design. DC, DB, BS, MJ, LH; PS, CS, PF, MM and TR involved in acquisition of data. DC, DB, AR, KGP, MT, MM and TR involved in analysis and interpretation of data. DC, MM and TR involved in drafting of the manuscript. DC, DB, BS, MJ, LH; PS, CS, AR, KGP, MT, PF, MM, MG and TR involved in critical revision of the manuscript for important intellectual content. All authors approved the final version and agreed to be accountable for all aspects of the work.

ORCID

David Chromy https://orcid.org/0000-0002-1807-8258
David J. M. Bauer https://orcid.org/0000-0002-9363-8518
Peter Ferenci https://orcid.org/0000-0003-2306-1992
Thomas Reiberger https://orcid.org/0000-0002-4590-3583

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