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Background. Direct-acting antivirals (DAAs) have substantially increased the rate of sustained virologic response in patients with hepatitis C compared with interferon therapy (IFN), while causing fewer adverse events. However, five recent case series and retrospective studies (Table 1) have reported a possible link between DAA treatment for hepatitis C and reactivation of varicella-zoster virus (VZV). Reported VZV reactivation rates in these studies were 0.23%, 0.72%, 1.50%, 1.74%, and 8.00%.

Methods. To further investigate these reported observations, we analyzed 37 prospective registrational DAA clinical trials, including 13,816 subjects in our analysis. Treatment arms were classified as DAA (N = 7,901), DAA + ribavirin (RBV) (N = 4,348), placebo (N = 997), DAA + IFN (N = 327), or IFN (N = 243). 1,068 (8%) subjects were HIV-coinfected, and 9,024 (65%) subjects were over age 50, both known risk factors for VZV reactivation. Herpes zoster (HZ) events occurring while on-treatment or during follow-up were identified using MedDRA preferred terms.

Results. We identified 36 (0.26%) subjects with HZ events. Thirty-two cases occurred during treatment, and 4 during follow-up. One event was considered severe, and the remaining were mild or moderate in severity. Of the 36 total cases reported, 11 (0.14%) were in DAA arms, 21 (0.48%) were in DAA+RBV arms, 4 (0.40%) were in placebo arms, and none were in DAA+IFN or IFN arms (Table 2). For a more direct comparison, we examined a subset of eight trials (N = 3835) containing both a DAA or DAA+RBV arm and a placebo arm. Of the 8 (0.21%) cases reported, 4 (0.14%) were in the DAA/DAA +RBV arms (N = 2838), and 4 (0.40%) were in the placebo arms (N = 997). While rates of VZV reactivation were increased for HIV-coinfected subjects (0.47% vs. 0.24%) and those over age 50 (0.31% vs. 0.17%) (Table 3), they remained similar to or lower than rates reported in previous studies (Table 1).

Conclusion. Data from prospective DAA clinical trials including 13,816 subjects do not provide evidence for an association between DAAs and VZV reactivation as reported in recent case series and retrospective studies. Low rates of VZV reactivation were observed, particularly in low-risk groups such as those below the age of 50, as would be expected in naturally occurring reactivation.

Table 1: Retrospective studies and case reports reporting a link between DAA treatment for hepatitis C and VZV reactivation.

Author	Journal	Publication Year	Population Size	HZ cases
Ghweil and Helal	*Infection and Drug Resistance*	2019	100	8 (8.00%)
Bruno et al.	*Clinical Gastroenterology and Hepatology*	2017	418	3 (0.72%)
Yokoo et al.	*Digestive and Liver Disease*	2017	268	4 (1.50%)
Kassas et al.	*Arab Journal of Gastroenterology*	2017	2133	5 (0.23%)
Perelló et al.	*Clinical Gastroenterology and Hepatology*	2016	576	10 (1.74%)

Table 2: VZV reactivation rates by treatment arm using data from 37 prospective clinical trials.

Treatment Arm	DAA N=7,901	DAA + RBV N=4,348	Placebo N=997	DAA + IFN N=327	IFN N=243	Total N=13,816
HZ Cases (%)	11 (0.14)	21 (0.48)	4 (0.40)	0	0	36 (0.26)

Table 3: Rates of VZV reactivation in subjects with HIV-coinfection and age>50, both known risk factors for VZV reactivation.

	HIV- coinfected		Age > 50	
	Yes N=1,068	No N=12,748	Yes N=9,024	No N=4,792
HZ Cases (%)	5 (0.47)	31 (0.24)	28 (0.31)	8 (0.17)

Disclosures. **All authors:** No reported disclosures.

293. Hepatitis C is now a Millennial Disease in Response to the Opioid Crisis: A Demographic Shift in Hepatitis C Infection

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Background. Previous research has shown millennials represent the fastest growing generation for those infected with the hepatitis C virus (HCV). Millennials are also a key driver in the opioid crisis, particularly in states of the Appalachian region including Kentucky. Despite research demonstrating a change in prevalence from baby boomers (born 1945–1965) to millennials (born 1980–1995), large representative studies providing evidence of the magnitude of this demographic shift are lacking in the United States. Our objective was to assess trends of HCV infection since 2016 in a large healthcare system located in an area of high prevalence of opioid use and HCV infection.

Methods. All individuals were screened for HCV infection in 2016, 2017, and 2018 within Norton Healthcare per standard risk-based criteria (e.g., injection drug users, baby boomers, etc.) as recommended by CDC, except for pregnant women who were universally screened since 2016. We tested for demographic shifts over time using longitudinal and time series analyses techniques

Results. A total of 86,243 individuals were screened for HCV infection from 2016 to 2018. Of those, 2,615 (3.0%) individuals screened positive for chronic HCV. The average age of those infected significantly decreased by an average of 3.7 years annually (from 47.3 years in 2016 to 39.9 years in 2018, $P < 0.001$). We forecast a plateau near the age of 28 years will be observed in just over 7 years. In addition, the proportion of millennials increased over time (33.6% in 2016, 42.4% in 2017 and 51.4% in 2018, $P < 0.001$), while baby boomers significantly decreased over time (44.0% in 2016, 38.8% in 2017, and 29.3% in 2018, $P < 0.001$). Lastly, over time, those with chronic HCV were more likely to be male (increasing from 49.6% to 54.4%, $P = 0.008$) and Hispanic (increasing from 1.6% to 17.7%, $P < 0.001$)

Conclusion. Our results suggest that HCV infection has become a predominately millennial disease, skipping a generation. These results correlate with trends seen with the opioid epidemic, which is driven by millennials. We conclude that the opioid crisis has led to a drastic demographic shift, and currently the typical HCV-infected individual is a younger male. Without interventions, this trend will continue for over seven years, plateauing near the demarcation of millennials and generation Z

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294. Hepatitis C Virologic Response in Hepatitis B and C Coinfected Persons Treated with Directly Acting Antiviral Agents: Results from ERCHIVES

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Background. There are scant data regarding hepatitis C (HCV) virologic response to directly acting antiviral agents (DAAs) in chronic hepatitis B (HBV) and HCV coinfected persons. HCV treatment response in those with spontaneously cleared HBV infection is unknown.

Methods. All HCV-infected persons treated with a DAA regimen in ERCHIVES were identified and categorized into HBV/HCV-coinfected (HBsAg, HBV DNA or both positive), HCV-monoinfected, and resolved HBV (isolated HBcAb+). SVR rates were determined and compared for all groups. A logistic regression model was used to determine factors associated with SVR.

Results. Among 115 HCV/HBV-coinfected, 38,570 HCV-monoinfected persons, and 13,096 persons with resolved HBV, 31.6% of HCV/HBV-coinfected, 24.6% of HCV-monoinfected and 26.4% with resolved HBV had cirrhosis at baseline. SVR was achieved in 90.4% of HCV/HBV-coinfected, 83.4% of HCV-monoinfected and 84.5% of those with resolved HBV infection ($P = 0.04$ HCV/HBV vs. HCV monoinfected). In a logistic regression model, those with HCV/HBV were more likely to achieve SVR compared with HCV monoinfected (OR 2.25, 95% CI 1.17, 4.31). For HCV/HBV coinfected, the SVR rates dropped numerically with increasing severity of liver fibrosis (P-value non-significant). Factors associated with a lower likelihood of attaining SVR included cirrhosis at baseline (OR 0.85, 95% CI 0.80, 0.92), diabetes (OR 0.93, 95% CI 0.87, 0.99) and higher pretreatment HCV RNA (OR 0.86, 95% CI 0.84, 0.87).

Conclusion. HBV/HCV-coinfected persons have higher overall SVR rates with newer DAA regimens. The virologic response is graded, with decreasing SVR rates with increasing degree of liver fibrosis as determined by the FIB-4 scores.

Table. Baseline characteristics and virologic response rates in persons treated with directly acting antiviral agents.

	HCV/HBV coinfected N=115 (Group A)	HCV monoinfected N=38,570 (Group B)	HCV with resolved HBV N=13,096 (Group C)	P-value A vs B	P-value A vs C	P-value B vs. C
Age in years, Mean (SD)	61.2 (7.3)	61.2 (7.4)	63.0 (5.3)	0.96	0.01	<.0001
Sex, male %	97.4%	96.5%	97.9%	0.80	0.51	<.0001
Race/ethnicity, %				0.02	<.0001	<.0001
White	58.3%	49.2%	40.3%			
Black	19.1%	33.0%	43.1%			
Hispanic	3.5%	2.6%	3.0%			
Other	19.1%	15.1%	13.6%			
Body mass index, kg/m² mean (SD)	27.8 (5.9)	28.2 (5.4)	28.0 (5.4)	0.46	0.68	0.003
Body mass index ≥ 30 kg/m², %	26.1%	32.1%	30.9%	0.19	0.31	0.01
FIB-4, median (IQR)	2.2 (1.6,3.7)	2.1 (1.4,3.2)	2.2 (1.6,3.4)	0.24	0.88	<.0001
FIB-4 category, %				0.22	0.31	<.0001
FIB-4 <1.45	21.9%	25.1%	20.2%			
FIB-4 1.46-3.25	46.5%	50.3%	53.4%			
FIB-4 >3.25	31.6%	24.6%	26.4%			
Diabetes, %	14.8%	15.7%	17.5%	0.90	0.54	<.0001
Hypertension, %	63.5%	65.1%	69.9%	0.70	0.15	<.0001
Cardiovascular disease diagnosis, %	75.7%	80.8%	79.0%	0.19	0.36	<.0001
Chronic kidney disease stage 3-5, %	31.9%	30.7%	33.4%	0.84	0.76	<.0001
Alcohol abuse or dependence, %	16.5%	20.8%	20.5%	0.30	0.35	0.48
Drug abuse or dependence, %	25.2%	23.3%	25.1%	0.66	1.00	<.0001
HCV RNA, log IU/mL, median (IQR)	8.6 (7.7,9.2)	8.1 (7.2,9.1)	8.2 (7.3,9.2)	0.005	0.03	<.0001
Sustained virologic response rates						
Overall	90.40%	83.40%	84.50%	0.04	0.08	0.002
By FIB-4 score						
FIB-4 < 1.45	100.0% (25)	83.9% (9,690)	84.6% (2,649)	0.02	0.02	0.33
FIB-4 1.46-3.25	90.6% (53)	84.1% (19,374)	85.2% (6,987)	0.2	0.27	0.03
FIB-4 > 3.25	86.1% (36)	81.5% (9,478)	83.1% (3,452)	0.47	0.63	0.04
P-values vs. FIB4<1.25						
FIB-4 1.46-3.25	0.17	0.68	0.54			
FIB-4 > 3.25	0.07	<.0001	0.09			

HBV, hepatitis B virus infection; HCV, hepatitis C virus infection;

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