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Hospitalizations for Hepatitis C in Mississippi, 2014–18: A Hidden Epidemic

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Goal: Utilizing Mississippi's hospital discharge data (HDD), we examined trends, demographics, comorbidities, in-hospital deaths, and hospital charges for hospitalizations with diagnoses for hepatitis C virus (HCV). Methods: We conducted a retrospective study of hospitalizations with primary or secondary HCV diagnoses. We performed descriptive and inferential statistical analyses using SAS 9.4. We compared categorical variables with chi-square tests and continuous variables with t-tests. Results: Between 2014 and 2018, patients hospitalized with an HCV diagnosis were more likely to have coexisting intravenous drug use (IDU) diagnoses compared to all other hospitalized patients (20.3% versus 3.3%; p < 0.001). From 2014 to 2018, hepatitis C infections associated with IDU spiked by 53.8%, fueling the overall increase in the number of hepatitis C hospitalizations in Mississippi. Almost one-third (31.8%) of all hepatitis C stays had a severe liver condition and 48.2% had nicotine dependence. The average charges for stays with coexisting HCV and decompensated cirrhosis were \$65,975. Conclusions: In Mississippi, there has been a rapid increase in HCV hospitalizations associated with IDU. In addition, HCV hospitalizations were associated with severe morbidity burden and high economic expense. These findings underscore the need for measures aimed at containing the spread of this dangerous but preventable infection.

Keywords: hepatitis C, intravenous drug use, hospitalizations, comorbidity, in-hospital mortality

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Introduction

Intravenous drug users are at risk for acquiring blood-borne infections, including hepatitis C (Bruneau at al., 2012). The escalating epidemic of injectable drugs, such as heroin and fentanyl, has fueled a parallel epidemic of hepatitis C (HCV). As a result, the annual incidence of acute hepatitis C more than doubled in 10 years in the United States, from 0.3 cases per 100,000 in 2004 to 0.7 cases per 100,000 in 2014 (Libel at al., 2018). This growing number of new cases presents a public health concern because hepatitis C is associated with substantial morbidity, including cirrhosis of the liver, liver cancer, liver failure, and increased demand for organ transplants (Mohamed at al., 2015). In short, hepatitis C is a major cause of preventable mortality that killed 20,000 Americans in 2013 (Ly at al., 2016).

Although hepatitis C is a nationally notifiable disease, collecting data on hepatitis C cases has been a challenge in Mississippi. Because of the lack of a systematic, statewide data collection system, little is known about the demographic distribution, comorbidity burden, medical complications, or social costs associated with this severe but preventable infection. To address this knowledge gap and learn more about the epidemiology of hepatitis C in Mississippi, we analyzed the state's hospital discharge data (HDD) for 2014–18. Specifically, we examined trends, demographics, comorbidities, in-hospital mortality, and resource utilization (e.g., hospital charges) for hepatitis C hospitalizations. Since hepatitis C virus is mostly transmitted via intravenous injections among drug users, we focused on evaluating the association between hepatitis C and intravenous drug use (IDU-HCV). In addition, we examined the number of HCV hospitalizations among two populations at risk for hepatitis C: baby boomers and the homeless (Neal, 2007). Because of contaminated blood transfusions before 1992, people born from 1945 to 1965 are five times more likely to have hepatitis C than other adults (Ryerson et al., 2016).

Methods

Study Design and Data

We conducted a retrospective study using statewide hospital discharge data. All non-federal hospitals in Mississippi, including mental health facilities, are required to submit their discharge data to the state's inpatient outpatient discharge data system. Compiled from medical claims, HDD contain information on patient demographics, residence, length of stay, total charges, clinical diagnosis, and procedures performed. The study population consisted of all hospitalizations with HCV diagnoses that occurred among residents and non-residents in Mississippi. To capture as many cases as possible, we included hospitalizations with primary or secondary HCV diagnoses.

The International Classifications of Diseases, Ninth and Tenth Revisions, Clinical Modification (ICD-9-CM and ICD-10-CM) were used to identify diagnoses for hepatitis C and coexisting

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medical conditions, including drug use disorder, liver illness, and homelessness. One limitation of the ICD-9-CM and ICD-10-CM classification systems is that they do not have codes specifying the route of drug admission. To address this challenge, we applied the diagnoses for three commonly injected substances (opioids, amphetamines, and cocaine) as a surrogate marker for IDU. Such an algorithm has been applied and validated in previous studies (Cooper at al., 2007).

Data Analyses

We performed descriptive statistical analyses of patients' demographic characteristics, comorbidity profiles, resource utilization, and outcomes of care. Inferential statistical analyses were performed to determine the association between IDU and HCV diagnoses, as well as to compare variables between different groups. We compared the demographic and comorbid characteristics between HCV hospitalizations with and without IDU diagnoses with chi-square tests. For comparison of continuous variables, we used independent t-tests. All statistical analyses were performed with SAS version 9.4.

Results

Association between Hepatitis C and Intravenous Drug Use

Between 2014 and 2018, there were a total of 66,297 hospitalizations attributable to IDU in Mississippi. During that time, the number of hepatitis C-associated stays was 22,522 and, among them, 4,581 (20.3%) had a coexisting IDU diagnosis. Inferential analyses revealed that patients hospitalized with an HCV diagnosis were more likely to have coexisting IDU-related diagnoses compared to all other hospitalized patients (20.3% versus 3.3%; p < 0.001).

Trends

In comparison with 2014, the number of IDU stays in 2018 rose from 10,491 to 15,396, representing a cumulative increase of 46.8% (an average annual increase of 10.0%). During the same time, the number of hospitalizations for hepatitis C increased by 3.1%, albeit with a small dip between 2017 and 2018 (Figure 1). This overall trend, however, differed for hepatitis C stays with and without IDU diagnoses. The cumulative increase for IDU-HCV hospitalizations was 53.8%, from 702 in 2014 to 1,080 in 2018, representing an annual average increase of 11.4%. By contrast, the trend in the number of non-IDU-HCV hospitalizations fluctuated only slightly. In fact, such hospitalizations declined cumulatively by 7.0% (an average annual decrease of 1.8%) during the same time. These statistics revealed that IDU-associated hepatitis C hospitalizations are driving up the overall hepatitis C hospitalization trend.

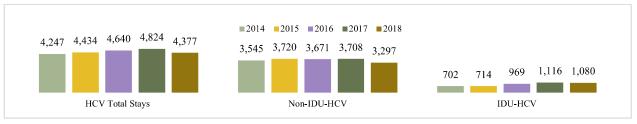


Figure 1. Number of hospital stays associated with hepatitis C in Mississippi, 2014–2018.

Multiple Drug Use

From 2014 to 2018 in Mississippi, among the 4,581 IDU-HCV hospitalizations, 2,636 (57.5%) had opioid-related diagnoses recorded; 1,765 (38.5%) had amphetamine-related diagnoses recorded; and 1,348 (29.4%) had cocaine-related diagnoses recorded. These drug groups are not mutually exclusive. In fact, multiple drug use was documented in 23.0% (1,055) of all IDU-HCV hospitalizations.

Demographics

Demographic analysis revealed that patients hospitalized with IDU-HCV diagnoses were, on average, 10 years younger than non-IDU-HCV patients (45.4 years versus 55.3 years; p < 0.001). In Mississippi, baby boomers (55–75 years of age) accounted for half (49.7%) of all hepatitis C stays but 28.2% of hepatitis C stays associated with IDU (Table 1). The majority of IDU-HCV stays occurred among the younger populations. The 18–54 age group accounted for 71.5% of all IDU-HCV hospitalizations. In fact, nearly one-quarter (24.3%) of all IDU-HCV stays were among the 18–34 age group. There were 14 hospitalizations associated with hepatitis C among the pediatric age group (0–17). Men comprised a higher proportion of all stays involving hepatitis C (58.0%) and accounted for the majority of IDU-HCV stays (56.5%). Compared with non-IDU-HCV, patients hospitalized with IDU-HCV were more likely to be Caucasian (82.6% versus 69.4%; p < 0.001).

Hepatitis C in the Homeless

In our data, a diagnostic code indicating homelessness (V60.0 and Z59.0) was recorded in 630 (2.8%) of all HCV-associated stays. Three-quarters of these patients (75.4%) were male and 80.5% were Caucasian. Nearly half of the stays (48.3%) with coexisting hepatitis C and homelessness were among self-paying patients, and 38.9% were covered by Medicaid or Medicare. Compared with non-IDU-HCV, patients hospitalized with IDU-HCV were more likely to have a code for homelessness (6.7% versus 1.8%; p < 0.001).

Table 1
Hepatitis C Hospitalizations: Demographic Characteristics in MS, 2014–2018 Combined

	All HCV Stays		IDU-HCV		Non-IDU-HCV		P Value
Gender	Number	Percent	Number	Percent	Number	Percent	
Female	9,458	42.0	1,992	43.5	7,466	41.6	P < 0.001
Male	13,064	58.0	2,589	56.5	10,475	58.4	P < 0.001
Race Group	Number	Percent	Number	Percent	Number	Percent	
Caucasian	16,225	72.0	3,782	82.5	12,443	69.4	
African American	5,784	25.7	731	16.0	5,053	28.2	P < 0.001
Other	513	2.3	68	1.5	445	2.4	1
Age Group (years)	Number	Percent	Number	Percent	Number	Percent	
0–17	14	0.1	6	0.1	8	0.0	
18–34	2,365	10.5	1,113	24.3	1,252	7.0	1
35–54	8,274	36.7	2,161	47.2	6,113	34.1	P < 0.001
55–75 (baby boomers)	11,186	49.7	1,291	28.2	9,895	55.2	1
76+	683	3.0	10	0.2	673	3.7	1
Homelessness	Number	Percent	Number	Percent	Number	Percent	
	630	2.8	305	6.7	325	1.8	P < 0.001

Comorbidity Burden in Patients Hospitalized with Hepatitis C

For the analysis of severe liver disease, we stratified data into five groups: hepatocellular carcinoma, liver transplant, liver cirrhosis (excluding alcoholic and biliary cirrhosis), advanced liver disease (i.e., liver failure, portal hypertension, ascites, varices, and hepato-renal syndrome), and alcoholic liver disease (i.e., alcohol-related fatty liver, hepatitis, unspecified liver damage, fibrosis, sclerosis, cirrhosis, and hepatic failure).

Nearly one-third (31.8%) of all hepatitis C stays had a severe liver condition on record: 18.7% had cirrhosis, 18.4% had advanced liver disease, and 3.0% had hepatocellular carcinoma. Despite recommendations for abstinence from alcohol, 10.5% of all hepatitis C hospitalizations had alcohol-related liver disease and 20.4% had alcohol use disorder. Half of all HCV hospitalizations (48.2%) had coexisting nicotine use disorder and 7.6% had coexisting cannabis use disorder. Less than 4.0% had coexisting HIV or HBV infections.

Compared to the non-IDU-HCV group, the IDU-HCV group was less likely to have liver cirrhosis, alcoholic liver disease, decompensated cirrhosis, and advanced liver disease. Non-injection substance use was highly prevalent among hepatitis C patients, particularly among those with coexisting IDU diagnoses. Comparative analysis uncovered that IDU-HCV stays were more likely to have coexisting tobacco use disorder (63.7% versus 44.3%; p < 0.001), alcohol use disorder (25.9% versus 19.1%; p < 0.001), and cannabis use disorder (21.5% versus 4.0%; p < 0.001) than non-IDU-HCV stays. The IDU-HCV cohort had a higher frequency of coexisting hepatitis B infection (4.9% versus 3.4%; p < 0.001). The proportion of coexisting HIV/AIDS, however, was similar between the two study groups (Table 2).

Table 2
Hepatitis C Hospitalizations with and without Intravenous Drug Use: Morbidity Burden and Outcomes of Care

	All Hepatitis C Stays		IDU-HCV Stays		Non-IDU-HCV		P Value
Liver-Related Morbidity	Number	Percent	Number	Percent	Number	Percent	
Cirrhosis of liver	4,221	18.7	415	9.1	3,806	21.2	P < 0.001
Alcoholic liver disease	2,363	10.5	221	4.8	2,142	11.9	P < 0.001
Decompensated cirrhosis	4,144	18.4	335	7.3	3,809	21.2	P < 0.001
Hepatocellular carcinoma	666	3.0	44	1.0	622	3.5	P < 0.001
All of the above conditions	7,172	31.8	705	15.4	6,467	36.1	P < 0.001
Non-Injection Drug Use-Related							
Disorders	Number	Percent	Number	Percent	Number	Percent	
Nicotine use disorder	10,857	48.2	2,916	63.7	7,941	44.3	P < 0.001
Alcohol use disorder	4,602	20.4	1,182	25.8	3,420	19.1	P < 0.001
Cannabis use disorder	1,708	7.6	985	21.5	723	4.0	P < 0.001
Coexisting HIV and HBV	Number	Percent	Number	Percent	Number	Percent	
HIV/AIDS	813	3.6	176	3.8	637	3.6	P = 0.345
Hepatitis B infection	840	3.7	224	4.9	616	3.4	P < 0.001
In-Hospital Deaths	Number	Percent	Number	Percent	Number	Percent	
	849	3.8	90	2.0	759	4.2	P < 0.001

ICD-9-CM/ICD-10-CM Codes for HCV: 07041; 07044; 07051; 07054; 0707; V0262; B1710; B1711; B182; B182; B1920; B1921; Z2252

 $\begin{array}{l} \textbf{ICD-9-CM/ICD-10-CM Codes for opioid use/abuse/poisoning: } 304.0; 304.7; 305.5; 965.0; E850.0; E850.1; E850.2; E935.0; E935.1; E935.2; F11: T400X1-T400X5; T401X1-T401X4; T402X1-T402X5; T403X1-T403X5; T404X1-T404X5; T40601-T40605; T40691-T40695 \end{array}$

ICD-9-CM/ICD-10-CM Codes for amphetamine use/abuse/poisoning: 304.4; 305.7; 969.7; E854.2; E939.7; F15; T43601-T43605; T43621-T43625; T43631-T43635; T43691-T43695

ICD-9-CM/ICD-10-CM Codes for cocaine use/abuse/poisoning: 304.2; 305.6; 970.81; F14: T405X1-T405X5

ICD-9-CM/ICD-10-CM Codes for Liver Comorbidities: Cirrhosis: 5715; K746; Hepatocellular carcinoma: 1550; C220; Alcohol liver disease: 5710; 5711; 5712; 5713; K70; Hepatic encephalopathy: 5722; K72; Varices: 4560; 4561; 4562; I85; Portal hypertension: 5723; K766; Ascites: 7895; R18 Hepatorenal syndrome: 5724; K767; Hepatic failure: K72; 5722; Liver transplant: V427, Z944

ICD-9-CM/ICD-10 Codes for Non-Injection Drug Use-Related Disorders: Nicotine Dependence: 3051; F17; Alcohol use disorder: 303; 3050; F10; Cannabis use disorder: 3052, 3043: F12

 $\textbf{ICD-9-CM/ICD-10 Codes for HBV} \ (0702:0703; B160; B161; B162; B169; B170; B180; B181; B191; \ Z2251; V06212) \ \textbf{and HIV/AIDS:} \ (042, V08, B20, Z21)$

In-Hospital Mortality

Between 2014 and 2018, there were 42,134 in-hospital deaths in Mississippi. Among those deaths, 849 (2.1%) were associated with HCV. The percent of in-hospital mortality was highest among patients with hepatocellular carcinoma: 11.0% of such stays had a documented death. Patients with decompensated cirrhosis and HCV had the second-highest mortality of 9.3%. Not surprisingly, hospital stays with diagnoses for alcoholic liver disease and hepatitis C also had a high mortality of 8.3%. The number of deaths among those with liver transplants was relatively low—a total of six deaths or 2.8% of all hospital stays with a diagnosis for liver transplant. Compared to the non-IDU-HCV group, in-hospital mortality was lower for the IDU-HCV group.

Hospital Charges

Between 2014 and 2018, the average charges for hepatitis C coexisting with liver cirrhosis or hepatocellular carcinoma were around \$53,000. The average charges for HCV and alcoholic liver disease were \$63,144; for HCV and decompensated cirrhosis, \$65,975; and for HCV and liver transplants, \$111,367. It is important to note that such patients may have had a history of liver transplants and not the actual procedure (Table 3).

Table 3
Hospitalizations for HCV and Comorbid Conditions; Number and Percent of Deaths, Mean and Total Charges in MS, 2014–2018

	Hospitalizations with Coexisting HCV	Number of Deaths	Percent of Cases with Recorded In- Hospital Deaths	Mean Charges	Total Charges, 2014–2018
Hepatocellular carcinoma	666	73	11.0%	\$53,218	\$35,443,015
Cirrhosis of liver	4,221	262	6.2%	\$53,232	\$224,692,803
Alcoholic liver disease	2,363	195	8.3%	\$63,144	\$149,208,502
Advanced liver disease	4,144	387	9.3%	\$65,975	\$273,400,350
Liver transplant	212	6	2.8%	\$111,367	\$23,609,737

Distribution of Hepatitis C Hospitalizations by Primary Expected Payer, 2018

The distribution of payers was different for stays with and without coexisting HCV and IDU diagnoses (Table 4). Compared with non-IDU-HCV, patients hospitalized with IDU-HCV were more likely to be uninsured (34.4% versus 17.0%; p < 0.001) in 2018. The proportion of patients with Medicare insurance, however, was lower among the IDU-HCV group than the non-IDU-HCV group (24.5% versus 43.0%; p < 0.001).

Trends in Payer Patterns

The number of Medicare patients hospitalized with an HCV diagnosis regardless of IDU status remained stable over time. Such stays accounted for 38.3% of all HCV admissions in 2014 and 38.5% in 2018 (Table 4). At the same time, the proportion of HCV hospitalizations increased for two groups of payers: self-paying patients accounted for 18.7% of all hepatitis C admissions in 2014 but for 21.3% in 2018; while privately insured patients accounted for 11.6% of all hepatitis C admissions in 2014 but for 13.4% in 2018. Among all major payers, only the state Medicaid program experienced a decline in the proportion of hepatitis C stays— from 26.3% in 2014 to 24.0% in 2018.

Table 4
Hepatitis C Hospitalizations: Percent of HCV Hospitalizations Primary Expected Payers, MS, 2014 and 2018

	All HCV Stays		IDU-HC	CV Stays	Non-IDU-HCV		
	2014	2018	2014	2018	2014	2018	
	%	%	%	%	%	%	
Medicare	38.3	38.5	26.4	24.5	40.7	43.0	
Medicaid	26.3	24.0	27.4	23.9	26.1	24.0	
Self-pay	18.7	21.3	32.6	34.4	15.9	17.0	
Private	11.6	13.4	9.1	15.6	12.1	12.7	
Other	5.1	2.8	4.6	1.6	5.2	3.2	

Discussion

Between 2014 and 2018, one out of every five patients hospitalized with hepatitis C in Mississippi had a concomitant diagnosis of IDU. Troublingly, one-quarter of all IDU-HCV hospitalizations were among young people between the ages of 18 and 34. This finding mirrors national trends: studies have identified that the majority of new HCV infections in the United States are among young intravenous drug users (Zibbell at al., 2018). The comorbidity burden among patients hospitalized with an HCV diagnosis was high; nearly one-third of such stays had a serious liver condition. The liver-related morbidity burden was smaller among IDU-HCV hospital stays compared to non-IDU-HCV stays. In part, this may be due to the fact that patients with IDU-HCV were younger than patients with non-IDU-HCV. For the same reason, in-hospital mortality was lower for the IDU-HCV group. The hospital charges associated with liver morbidity were high. In addition, more than one-fifth of all charges occurred among self-paying patients. The serious comorbidity burden among patients suffering from hepatitis C and the associated high cost for their treatment reveal that the medical and economic consequences of the ongoing intravenous drug abuse are far-reaching.

From 2014 to 2018, hepatitis C infections associated with IDU nearly doubled, fueling the overall increase in the number of stays for hepatitis C in Mississippi. The parallel increase in drug abuse and blood-borne infections suggests a causal relation and underlines the importance of building statewide programs for preventing, diagnosing, and treating drug-associated infectious diseases. These programs could implement such public health and clinical measures as building an extensive surveillance system for drug-related illnesses, encouraging legislative initiatives for harm-reduction programs, enhancing diagnostic tools for suspected drug-associated infections, and improving treatment options for patients with drug dependence.

As research suggests, the use of contaminated needles has been the main force behind the growing number of hepatitis C cases across the nation as this infection is transmitted primarily through the parenteral route. For example, between 38.1% and 68.0% of injection drug users also have co-existing hepatitis C (Degenhardt at al., 2017). In addition to the mode of transmission, the chronic nature of this disease has resulted in high prevalence rates across the nation. Hepatitis C infection is, therefore, an evolving national epidemic, with an estimated 2.4 million Americans living with this disease in 2016 (Hofmesiter at al., 2016). Most likely, the high prevalence of hepatitis C and growing use of cheap heroin and synthetic fentanyl will continue to drive up the incidence of hepatitis C both nationally and in Mississisppi.

Data Limitations

Statewide hospital discharge data have some limitations. This data source does not include discharges from federal facilities, including Veterans Health Administration hospitals or prison facilities. Consequently, we could not account for hepatitis C discharges from such facilities.

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Due to the stigmatization surrounding drug use behaviors, patients may not report drug use during their hospitalizations. Hence, drug-related diagnoses may not always be recorded in healthcare data. Because of the above-mentioned data shortcomings, the number of HCV hospitalizations with an IDU diagnosis may be underestimated in this study.

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