Increasing Prevalence of Hepatitis C among Hospitalized Children Is Associated with an Increase in Substance Abuse

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Objective To evaluate the impact of substance abuse on pediatric hepatitis C virus (HCV) prevalence, we examined geographic and demographic data on inpatient hospitalizations in children with HCV.

Study design We examined hospitalizations in children using the Kids' Inpatient Database, a part of the Healthcare Cost and Utilization Project. We identified cases using the *International Classification of Diseases*, 9th edition, codes for HCV infection during 2006, 2009, and 2012. Nonparametric tests for trend were used to calculate trend statistics.

Results From 2006 to 2012 nationally, the number of hospitalizations of children with HCV increased 37% (2.69 to 3.69 per 10 000 admissions; $P < .001$). The mean age of children hospitalized was 17.6 years (95% CI, 17.4-17.8). HCV cases among those 19-20 years of age represented 68% of the total HCV diagnoses, with a 54% increase over the years sampled ($P < .001$ for trend). The burden of HCV in children was highest in whites, those in the lowest income quartile, and in the Northeast and Southern regions of the US (all $P < .0001$). The prevalence of substance use among children with HCV increased from 25% in 2006 to 41% in 2012 ($P < .001$).

Conclusion The increases of HCV in hospitalized children are largely in teenagers, highly associated with substance abuse, and concentrated in Northeast and Southern states. These results strongly suggest that public health efforts to prevent and treat HCV will also need to include adolescents. *(J Pediatr 2017;■■:■■-■■).*

Hepatitis C virus (HCV) is well-known worldwide as a cause of chronic liver disease in adults and contributes to significant healthcare use.[1,2] After a sustained decline in new HCV cases, in recent years there has been a significant increase in HCV incidence in adults in many areas, primarily associated with the use and abuse of intravenous heroin and prescription opioids.[3-5] What is less well-known is the current burden of HCV in children and how the substance abuse related HCV cases among adults has affected the pediatric population.

There are approximately 50 000 children living with chronic HCV in the US and 11 million children under 15 years old worldwide.[6,7] As direct-acting antivirals (DAAs) are approved for adolescents and continue to be studied in younger children, defining the burden among children now will be essential to break the cycle of HCV transmission.[8,9] As the costs and benefits of DAA use in children are considered, the lack of information about the current burden of HCV becomes more apparent. To help address this knowledge gap, we sought to first define the burden of inpatient HCV among pediatric populations, risk factors for infection, as well as the socioeconomic and geographical characteristics of disease.

Methods

We examined hospitalizations in children using the Kids' Inpatient Database (KID), a part of the Healthcare Cost and Utilization Project, Agency for Healthcare Research and Quality, in accordance with their data use agreement. The KID is the largest publicly available pediatric inpatient database in the United States; all payors are included. The KID contains de-identified patient- and hospital-level discharge data across 44 states and more than 4100 community hospitals in 3-year increments. Data from 2006, 2009, and 2012 were included in this analysis. Approximately 3 million discharges are collected annually accounting for a weighted estimation of 7 million pediatric hospitalizations. KID is designed to facilitate national and regional studies of both rare and common pediatric diseases.[10] Of note, state-level federal information process standards identifiers were included in the 2006 and 2009 datasets, but were removed from the 2012 version.

We chose to compare HCV hospitalization with hospitalizations for appendectomy as a control group, hypothesizing that appendicitis represents a common pediatric medical problem that is not bound by geographic or demographic

DAAs	Direct-acting antivirals
HCV	Hepatitis C virus
KID	Kids' Inpatient Database

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boundaries and has been relatively stable in incidence over time. Primary and secondary *International Classification of Diseases,* 9th edition, diagnosis codes were used for identifying patients with HCV (070.41, 070.44, 070.51, 070.54, 070.70, 070.71, V0262) and patients undergoing appendectomy (540.0, 540.1, 540.9). Additionally, we used *International Classification of Diseases,* 9th edition, codes identifying patients with substance abuse (304.0×, 305.5×, 305.9×). We hypothesized that differential age distributions existed between patients with HCV and patients with appendectomies. As a result, we performed frequency matching of HCV and randomly sampled appendectomy cases using a 1:3 ratio within each *a priori* defined age category: ≤1, 2-3, 4-6, 7-9, 10-12, 13-15, 16-18, and ≥19 years of age.

Statistical Analyses

The patient discharge weight with a primary sampling unit specification and strata indicator were used to account for the complex survey design of KID. We report unadjusted and adjusted statistics comparing demographic characteristics and substance abuse between HCV and appendectomy patients. Taylor series linearization variance estimation was used for standard error calculations. Statistical significance was determined from a Wald test, which was based on an adjusted F statistic. Multivariable logistic models were used to predict the odds of HCV and the odds of substance abuse. All analyses were conducted using SAS (v9.4, SAS Institute Inc, Cary, North Carolina).

We used the 2009 KID dataset to obtain state-specific rates for HCV and substance abuse, per 10 000 hospitalizations. This dataset was selected because it is the most recent dataset with state and federal information process standards identifiers. We ran a Pearson product-moment correlation to determine the relationship between state-level HCV and substance abuse. Last, we provide choropleth maps to demonstrate regional variability across the US.

Results

Patient demographics for all children hospitalized with HCV and appendicitis are shown in **Table I**. In the pooled analysis

Table I. Demographic comparisons between HCV and appendicitis

Demographics	HCV				Appendectomy				
	Weighted Count	Col Percentage	95% CI Lower	95% CI Upper	Weighted Count	Col Percentage	95% CI Lower	95% CI Upper	Rao-Scott χ^2
Patient Age (y)									
≤1	268	4.14	3.46	4.81	826	4.34	3.84	4.84	.9998
2-3	235	3.63	2.76	4.51	674	3.54	3.15	3.93	
4-6	72	1.12	0.76	1.48	215	1.13	0.94	1.32	
7-9	55	0.85	0.56	1.15	169	0.89	0.72	1.06	
10-12	97	1.50	1.06	1.94	285	1.50	1.28	1.72	
13-15	161	2.48	1.91	3.05	481	2.53	2.24	2.82	
16-18	1356	20.93	19.42	22.43	3948	20.76	20.03	21.48	
>18	4233	65.35	63.44	67.26	12425	65.32	64.30	66.33	
Sex									
Male	2128	32.86	31.14	34.57	10541	55.41	54.53	56.30	<.0001
Female	**4345**	**67.07**	**65.35**	**68.78**	8000	42.05	41.19	42.92	
Unknown	5	0.07	0.00	0.16	482	2.53	2.23	2.84	
Race/ethnicity									
White	**3942**	**60.86**	**58.57**	**63.15**	9136	48.03	46.83	49.22	<.0001
Black	592	9.13	7.87	10.40	1356	7.13	6.62	7.64	
Hispanic	629	9.70	8.33	11.08	4259	22.39	21.31	23.47	
Asian/PI	67	1.04	0.65	1.43	404	2.12	1.85	2.40	
Native American	50	0.77	0.49	1.05	169	0.89	0.68	1.10	
Other	227	3.50	2.73	4.27	796	4.18	3.72	4.65	
Unknown	971	14.99	13.19	16.80	2903	15.26	14.31	16.21	
Census region									
Northeast	**1745**	**26.93**	**24.71**	**29.16**	3799	19.97	18.99	20.95	<.0001
Midwest	1232	19.02	17.24	20.80	3354	17.63	16.75	18.52	
South	**2555**	**39.45**	**37.08**	**41.81**	6354	33.40	32.09	34.71	
West	946	14.60	12.98	16.21	5516	29.00	27.76	30.24	
Zip code income quartile									
1	**2374**	**36.66**	**34.68**	**38.63**	5198	27.32	26.28	28.37	<.0001
2	1509	23.29	21.70	24.89	4420	23.24	22.39	24.08	
3	1355	20.92	19.45	22.39	4444	23.36	22.49	24.23	
4	1029	15.89	14.46	17.32	4591	24.14	23.12	25.15	
Unknown	210	3.24	2.61	3.87	370	1.94	1.64	2.25	
Diagnosis code for substance abuse									
No	4310	66.53	64.65	68.41	18985	99.80	99.72	99.88	<.0001
Yes	**2168**	**33.47**	**31.59**	**35.35**	38	0.20	0.12	0.28	

Bold indicates subgroup with significant difference in statistical analysis.
PI, Pacific Islander.

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