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Prevalence of indications for adult hepatitis A vaccination among hepatitis A outbreak-associated cases, Three US States, 2016–2019

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Abstract

Background: Safe and effective hepatitis A vaccines have been recommended in the United States for at-risk adults since 1996; however, adult vaccination coverage is low.

Methods: Among a random sample of adult outbreak-associated hepatitis A cases from three states that were heavily affected by person-to-person hepatitis A outbreaks, we assessed the presence of documented Advisory Committee on Immunization Practices (ACIP) indications for hepatitis A vaccination, hepatitis A vaccination status, and whether cases that were epidemiologically linked to an outbreak-associated hepatitis A case had received postexposure prophylaxis (PEP).

Results: Overall, 74.1% of cases had a documented ACIP indication for hepatitis A vaccination. Fewer than 20% of epidemiologically linked cases received PEP.

Conclusions: Efforts are needed to increase provider awareness of and adherence to ACIP childhood and adult hepatitis A vaccination and PEP recommendations in order to stop the current person-to-person hepatitis A outbreaks and prevent similar outbreaks in the future.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Keywords

Hepatitis A; Hepatitis A vaccines; Postexposure prophylaxis; Disease outbreaks; United States

1. Introduction

Hepatitis A is a vaccine-preventable disease of the liver, typically acquired through fecal-oral transmission of the hepatitis A virus (HAV) from direct person-to-person contact or consumption of contaminated food or water. Hepatitis A (HepA) vaccines are safe and highly effective (94%–100% efficacy in protecting against clinical hepatitis A with single-antigen HepA vaccines) and were first licensed in the United States in 1995 [1–3]. In 1996, the Advisory Committee on Immunization Practices (ACIP) recommended vaccination for adults at increased risk for HAV infection or adverse consequences of infection (e.g., people who use drugs, men who have sex with men [MSM], international travelers, and people with chronic liver disease) [3]. Recently, ACIP expanded the indications for adult hepatitis A vaccination to include people experiencing homelessness (2019) and people living with HIV (2020) [3].

Postexposure prophylaxis (PEP) with single-antigen HepA vaccine or immune globulin effectively prevents infection with HAV when administered within two weeks of exposure [3]. ACIP recommends PEP as soon as possible for adults exposed to HAV within the past two weeks who have not previously completed the HepA vaccine series [3]. The efficacy of PEP administered more than two weeks after exposure has not been established.

Since 2016, the United States has experienced person-to-person hepatitis A outbreaks that are unprecedented in the vaccine era. Infections have spread primarily through close contact among people who use drugs—a group recommended for hepatitis A vaccination by ACIP for 25 years—and people experiencing homelessness [3,4]. As of September 10, 2021, state health departments reported >42,000 outbreak-associated cases [4]. We sought to identify opportunities for improving adult hepatitis A vaccination coverage before and during the ongoing person-to-person hepatitis A outbreaks.

2. Methods

Previously, we conducted a cross-sectional observational study of hepatitis A outbreak-associated cases with onset between July 1, 2016 and June 10, 2019 [5]. Eligibility for inclusion in the analysis was residency in Kentucky, Michigan, or West Virginia and designation by the respective health department as a person-to-person outbreak-associated hepatitis A case. For that analysis, state outbreak and hospital records were abstracted for a 10% simple random sample of outbreak-associated hepatitis A cases from three heavily-affected states.

For this analysis, we examined data collected during the cross-sectional observational study for the presence of documented ACIP indications for hepatitis A vaccination among adults, hepatitis A vaccination status, and whether cases that were epidemiologically linked to an outbreak-associated hepatitis A case had received PEP. ACIP indications were

assessed retrospectively. We examined the presence of all ACIP indications for hepatitis A vaccination in the current 2020 ACIP recommendations, including homelessness and living with HIV, which were not in place during the study period. Hepatitis A vaccination status was based on self-report or documentation (in the medical record or state immunization registry) of ever receiving a HepA dose. Cases were considered epidemiologically linked if they were a close contact (e.g., household or sexual) of a known hepatitis A outbreak-associated case.

We calculated descriptive statistics detailing potential opportunities for improving adult hepatitis A vaccination before and during the ongoing person-to-person hepatitis A outbreaks. Percentages were calculated by using all participants (including those with missing data) in the denominator to err on the side of generating conservative estimates.

CDC determined this analysis, using existing deidentified data provided by jurisdictions as part of hepatitis A outbreak investigations and response efforts, did not constitute research involving human subjects; IRB review was not required.

3. Results

We identified 817 hepatitis A outbreak-associated cases via generation of the 10% random sample. Of these, 812 were adults with documented information on ACIP indications for hepatitis A vaccination (467 from Kentucky, 92 from Michigan, and 253 from West Virginia). No cases included in the analysis had verifiable documentation of having received the full 2-dose hepatitis A vaccination series before becoming infected. One hundred and forty-one cases were epidemiologically linked to a known hepatitis A case.

Overall, 74.1% (602/812) of adult cases had a documented ACIP indication for hepatitis A vaccination (Table 1). When restricted to ACIP recommendations during the study period, 73.2% of adult cases had documentation of an ACIP indication for hepatitis A vaccination (73.0% of Kentucky residents [341/467], 68.5% of Michigan residents [63/92], and 75.1% of West Virginia residents [190/253]) (Table 1). Two longstanding ACIP indications for hepatitis A vaccination (i.e., those recommended since 1996) were the most prevalent indications for hepatitis A vaccination in the study population: use of injection or noninjection drugs (459/812, 56.5%) and preexisting chronic liver disease (437/812, 53.8%) (Table 1). The other longstanding ACIP indications were less common in the study population: MSM was identified for 2.9% of male cases (15/509) while international travel was identified for 0.1% of cases (1/812) (Table 1). Newer ACIP indications for hepatitis A vaccination that were approved after the study period ended but applied retrospectively to the analytic sample included homelessness (92/812, 11.3%) and living with HIV (2/812, 0.2%) (Table 1). Overall, more than one-third of adult cases had multiple ACIP indications for hepatitis A vaccination (42.1% overall [342/812]; 42.4% of Kentucky residents [198/467], 33.7% of Michigan residents [31/92], and 44.7% of West Virginia residents [113/253]) (Table 1).

Among 141 hepatitis A outbreak-associated cases epidemiologically linked to a known hepatitis A case, 8.5% (12/141) received PEP (Table 2). Of those epidemiologically linked

cases with known PEP status, 13.6% of Kentucky residents (6/44), 21.4% of Michigan residents (3/14), and 60.0% of West Virginia residents (3/5) received PEP (Table 2). However, 66.7% of PEP recipients in each state received PEP outside the recommended window (Table 2).

4. Discussion

Since 2016, person-to-person hepatitis A outbreaks that are unprecedented in the vaccine era have impacted the United States. We analyzed a random sample of adult hepatitis A outbreak-associated cases from three heavily-affected states and found that there were substantial opportunities for improving adult hepatitis A vaccination – both before and during the outbreaks.

Approximately three-quarters of the adult cases identified had a documented ACIP indication for hepatitis A vaccination, yet none had verifiable documentation of receiving the 2-dose vaccination series before infection. Consistent with our study results, self-reported hepatitis A vaccination coverage among adults in the United States is low, even among risk groups specifically recommended for hepatitis A vaccination by ACIP. In 2017, according to data from the National Health Interview Survey, only 10.9% of adults ≥19 years reported receiving ≥2 HepA doses [6]. The same survey also examined hepatitis A vaccination coverage specifically among adults ≥19 years with chronic liver conditions and found that coverage improved compared to the general adult population, but was still low at 20.8% [6]. According to a recent National Health and Nutrition Examination Survey study, among US-born adults aged ≥20 years during 2007–2016, 24.9% of participants with hepatitis B or hepatitis C, 26.9% of participants who reported injection drug use, and 34.8% of participants who identified as MSM reported ever being vaccinated against hepatitis A, respectively [7].

The risk-based ACIP recommendations for adult hepatitis A vaccination involve hard-to-reach populations that might have limited access to routine health care or preventive services. Since 2016, jurisdictions—including the three involved in this study—have developed and implemented nontraditional vaccination strategies and innovative staffing models (e.g., holding satellite vaccination clinics at facilities providing services to hard-to-reach populations, such as correctional facilities, syringe services programs, and homeless shelters; and expanding the authority of emergency medical technicians and pharmacists to administer hepatitis A vaccine) to provide HepA vaccine to adults recommended for vaccination during the person-to-person hepatitis A outbreaks [8–10]. However, such efforts are labor and resource intensive.

The ACIP has recommended universal hepatitis A vaccination of all children aged 12–23 months since 2006 [11]. This recommendation has the potential to improve population coverage by eliminating barriers associated with risk-based adult hepatitis A vaccination. However, according to the most recent National Immunization Survey-Child data available, coverage with ≥2 HepA doses by age 35 months was only 76.9%, one of the lowest series completion coverage rates among ACIP-recommended childhood vaccinations [12]. Despite the low national coverage rate, from 2017 to 2019, the coverage rate with

≥2 HepA doses among children 19–35 months of age held steady in West Virginia and improved approximately 8% in Kentucky and 18% in Michigan, suggesting that public health messaging about the hepatitis A outbreaks improved provider awareness of the need to vaccinate against hepatitis A [CDC, unpublished data]. State vaccination requirements can be important tools for achieving and maintaining high vaccination coverage rates. As of 2020, though, only 24 states had a childhood (childcare or school) hepatitis A vaccine mandate [13]. Although the participants in our study cohort were too old to benefit from the universal childhood hepatitis A vaccination recommendation, comprehensive implementation of the universal childhood recommendation (and the 2020 catch-up recommendation for those aged 2–18 years [3]) will be vitally important to prevent a future recurrence of the widespread person-to-person hepatitis A outbreaks currently affecting the United States.

Despite being highly effective when administered as recommended within two weeks of exposure, PEP was infrequently administered to cases we identified that were epidemiologically linked to known outbreak-associated hepatitis A cases. This may be indicative of the difficulty public health staff experienced in attempting to reach the underserved populations most heavily affected by these outbreaks, and the reluctance of outbreak-associated hepatitis A cases to identify their potential contacts by name. When PEP was administered, it was given outside the recommended window twice as often as it was given appropriately within the recommended window. These findings underscore the need to improve awareness of hepatitis A PEP recommendations among public health professionals and clinicians.

Our study has several limitations. First, risk factor data abstracted to determine the presence of documented ACIP indications for hepatitis A vaccination were largely self-reported and subject to recall and social desirability biases. Consequently, the results may underestimate the actual prevalence of preexisting ACIP indications for hepatitis A vaccination. We conducted a sensitivity analysis restricted to those with non-missing data and found that 97.4% of cases eligible for inclusion had documentation of an ACIP indication for hepatitis A vaccination. Second, we retrospectively assessed documentation of the most recent ACIP indications for vaccination (e.g., people experiencing homelessness and people living with HIV). Although these were not official ACIP recommendations for adult hepatitis A vaccination during the study period, CDC did provide an outbreak-specific recommendation in 2017 to vaccinate people experiencing unstable housing or homelessness against hepatitis A in the context of person-to-person hepatitis A outbreaks [4,14]. Additionally, the difference between the prevalence of any ACIP indication restricted to those officially in effect during the study period versus any ACIP indication assessed overall was approximately 1%, suggesting that including the retrospective assessment of the most recent indications for vaccination did not substantially alter the study results. Third, it is possible that the hepatitis A vaccination status of some adult hepatitis A outbreak-associated cases included in the analysis was misclassified. Health department staff conducting case investigations inquired about hepatitis A vaccination status, cross-referenced state immunization registries, and reviewed medical records when available. However, some outbreak-associated cases were lost to follow-up and unable to be interviewed. Fourth, whether PEP was offered (and patient responses to such offers) was not consistently

captured. As a result, we were unable to account for attempted PEP administration that was refused by patients in the PEP analysis. Finally, the representativeness of the study might be limited because only three states experiencing person-to-person hepatitis A outbreaks were included. However, Kentucky, Michigan, and West Virginia accounted for 40% of publicly-reported person-to-person hepatitis A cases nationally at the end of the study period in June 2019.

In summary, we identified substantial opportunities for improving adult hepatitis A vaccination, both before and during the person-to-person hepatitis A outbreaks in Kentucky, Michigan, and West Virginia. Nearly 75% of the adult cases included in this study had a documented indication for vaccination; appropriate, timely vaccination could have prevented substantial hepatitis A morbidity and mortality during the person-to-person hepatitis A outbreaks. Continued implementation of nontraditional vaccination strategies should be prioritized to reach at-risk adult populations involved in the ongoing outbreaks. Fewer than 20% of patients who should have received PEP because they were epidemiologically linked to a known hepatitis A case received PEP; of those who did, two-thirds received PEP outside the recommended two-week window when PEP is effective. Efforts are needed to increase provider awareness of and adherence to ACIP childhood and adult hepatitis A vaccination and PEP recommendations in order to stop the current person-to-person hepatitis A outbreaks and prevent similar outbreaks in the future.

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Abbreviations:

HAV	hepatitis A virus
HepA	hepatitis A vaccine(s)
ACIP	Advisory Committee on Immunization Practices
MSM	men who have sex with men
PEP	postexposure prophylaxis

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Table 1

Prevalence of documented Advisory Committee for Immunization Practices indications for hepatitis A vaccination among adult hepatitis A outbreak-associated cases – Kentucky, Michigan, and West Virginia, 2016–2019.[1]

ACIP indication for hepatitis A vaccination	Overall (n = 812), n (%)	Kentucky (n = 467), n (%)	Michigan (n = 92), n (%)	West Virginia (n = 253), n (%)
Specific indications in effect during study period				
People traveling to or working in countries that have high or intermediate endemicity of infection	1 (0.1)	0 (0.0)	1 (1.1)	0 (0.0)
Men who have sex with men[2]	15 (2.9)	4 (1.4)	11 (17.5)	0 (0.0)
People who use injection or noninjection drugs	459 (56.5)	260 (55.7)	47 (51.1)	152 (60.1)
People with chronic liver disease[3]	437 (53.8)	260 (55.7)	32 (34.8)	145 (57.3)
Any indication	594 (73.2)	341 (73.0)	63 (68.5)	190 (75.1)
Multiple indications	315 (38.8)	181 (38.8)	27 (29.3)	107 (42.3)
Specific indications implemented after the study period and assessed retrospectively				
People experiencing homelessness	92 (11.3)	50 (10.7)	10 (10.9)	32 (12.6)
People living with HIV	2 (0.2)	1 (0.2)	1 (1.1)	0 (0.0)
Any indication	94 (11.6)	51 (10.9)	11 (12.0)	32 (12.6)
Multiple indications	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Overall				
Any indication	602 (74.1)	346 (74.1)	64 (69.6)	192 (75.9)
Multiple indications	342 (42.1)	198 (42.4)	31 (33.7)	113 (44.7)

[1] Overall and state-stratified number of adult hepatitis A cases with specified ACIP indication among total.

[2] Restricted to adult male cases. Overall n = 509; Kentucky n = 295, Michigan n = 63, West Virginia n = 151.

[3] Defined, for the purposes of the analysis, as history of hepatitis B (laboratory evidence of prior exposure or current infection, or hepatitis B diagnosed in the medical record), history of hepatitis C (laboratory evidence of prior exposure or current infection, or hepatitis C diagnosed in the medical record), alcoholic liver disease, nonalcoholic fatty liver disease, autoimmune hepatitis, or cirrhosis.

Table 2

Postexposure prophylaxis administration among hepatitis A outbreak-associated cases epidemiologically linked to a known hepatitis A case – Kentucky, Michigan, and West Virginia, 2016–2019 (n = 141).[1]

	Overall, n (%)	Kentucky, n (%)	Michigan, n (%)	West Virginia, n (%)
Proportion of epidemiologically linked outbreak-associated hepatitis A cases that did not receive PEP	51 (36.2)	38 (52.8)	11 (78.6)	2 (3.6)
Proportion of epidemiologically linked outbreak-associated hepatitis A cases that did receive PEP	12 (8.5)	6 (8.3)	3 (21.4)	3 (5.5)
PEP was administered outside the recommended window[2]	8 (66.7)	4 (66.7)	2 (66.7)	2 (66.7)
Proportion of epidemiologically linked outbreak-associated hepatitis A cases with unknown PEP status	78 (55.3)	28 (38.9)	0 (0.0)	50 (90.9)

Abbreviations: PEP, postexposure prophylaxis.

[1]Restricted to those who were designated as epidemiologically linked to a known hepatitis A outbreak-associated case (n = 141 overall; n = 72 for Kentucky, n = 14 for Michigan, n = 55 for West Virginia).

[2]Restricted to those epidemiologically linked outbreak-associated hepatitis A cases that did receive PEP.