Title

Meningococcal Disease in Persons With HIV Reported Through Active Surveillance in the United States, 2009-2019.

Journal

Open Forum Infectious Diseases, 11(1)

ISSN

2328-8957

Authors

Rudmann, Keegan

Cooper, Gabrielle

Marjuki, Henju

et al.

Publication Date

2024

DOI

10.1093/ofid/ofad696

Peer reviewed

Open Forum Infectious Diseases

BRIEF REPORT

Meningococcal Disease in Persons With HIV Reported Through Active Surveillance in the United States, 2009–2019

Keegan C. Rudmann,[1] Gabrielle Cooper,[1,©] Henju Marjuki,[1] Arthur Reingold,[2] Meghan Barnes,[3] Susan Petit,[4] Ashley Moore,[5] Lee H. Harrison,[6] Ruth Lynfield,[7] Sarah A. Khanlian,[8] Bridget J. Anderson,[9] Tasha Martin,[10] William Schaffner,[11] Lucy A. McNamara,[1] and Amy B. Rubis[1]

[1]Division of Bacterial Diseases, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia, USA (now with Banner Health, Phoenix, Arizona, USA), [2]School of Public Health, University of California, Berkeley, California, USA, [3]Colorado Department of Public Health and Environment, Denver, Colorado, USA, [4]Connecticut Department of Public Health, Hartford, Connecticut, USA, [5]Georgia Department of Public Health, Atlanta, Georgia, USA, [6]Departments of Epidemiology and Medicine, University of Pittsburgh, Pittsburgh, Pennsylvania, USA, [7]Minnesota Department of Health, St. Paul, Minnesota, USA, [8]University of New Mexico Emerging Infections Program, Albuquerque, New Mexico, USA, [9]New York State Department of Health, Albany, New York, USA, [10]Oregon Health Authority Public Health Division, Portland, Oregon, USA, and [11]Department of Preventive Medicine, Vanderbilt University Medical Center, Nashville, Tennessee, USA

Persons with HIV (PWH) are at increased risk for bacterial infections, and previous publications document an increased risk for invasive meningococcal disease (IMD) in particular. This analysis provides evidence that PWH face a 6-fold increase in risk for IMD based on Active Bacterial Core surveillance data collected during 2009–2019.

Keywords. invasive meningococcal disease; *Neisseria meningitidis*; people with HIV.

Bacterial infections account for 15% of hospitalizations in people with HIV (PWH) [1], and previous studies have shown that even PWH who are treated with combination antiretroviral therapy (cART) in the United States still experience a risk of invasive pneumococcal disease that is 35-fold higher than the general population [2]. The risk of invasive meningococcal disease (IMD), caused by the bacterium *Neisseria meningitidis*, has been reported to range from 2.5- to 13-fold higher in PWH compared with people not known to have HIV (non-PWH) [3–5]. Among PWH, a low CD4 count or high viral load has been shown to be associated with an increased risk of IMD [3]. A previous analysis using IMD data from Active Bacterial Core surveillance (ABCs) identified a 13-fold higher risk for IMD in PWH meeting the Centers for Disease Control and Prevention (CDC) HIV stage 3 (AIDS) surveillance case definition [6] during 2000–2008 (relative risk, 12.9; 95% CI, 7.9–20.9) [7]. Data are limited on the risk of IMD among all PWH in the United States.

In 2016, the US Advisory Committee on Immunization Practices (ACIP) recommended routine quadrivalent meningococcal conjugate (MenACWY) vaccination among persons aged ≥2 months with HIV infection [3].

This analysis serves as a follow-up to the previous evaluation of IMD risk in PWH to better understand how the declining incidence of IMD in the United States, along with the 2016 ACIP MenACWY recommendation for PWH, has affected IMD risk in PWH.

METHODS

IMD cases identified through ABCs during 2009–2019 were reviewed. ABCs is an active, population- and laboratory-based surveillance system that is part of the CDC's Emerging Infections Program (EIP). The ABCs surveillance area includes 10 sites: California (3 San Francisco Bay counties), Colorado (5 Denver-area counties), Connecticut, Georgia, Maryland, Minnesota, New Mexico, New York (15 Rochester- and Albany-area counties), Oregon, and Tennessee (11 counties in 2009; 20 counties during 2010–2019). A case of IMD was defined as isolation of *N. meningitidis* from a normally sterile site or detection of pathogen-specific nucleic acid in a specimen obtained from a normally sterile body site using a validated molecular test in a resident of one of the surveillance areas. Species and serogroup were determined by state public health laboratories and confirmed at the CDC using slide agglutination, polymerase chain reaction (PCR), and/or whole-genome sequencing when an isolate was available.

Data collection forms were completed for IMD patients reported to have HIV infection. These forms collected clinical and epidemiologic information including HIV disease–related data (ie, CD4 cell counts and AIDS-defining conditions), physical examination at presentation, comorbidities, IMD risk factors including medical conditions that increase risk for IMD (asplenia and complement deficiency), meningococcal vaccination history, and any hospital complications of IMD. Individuals with a CD4 count ever <200 cells/μL or a history of an AIDS-defining condition were identified as meeting the CDC AIDS surveillance case definition [6]. Concurrent CD4 cell counts were defined as a CD4 count dated within 3 months before the date of IMD presentation, performed during the hospitalization, or reported in the chart as current.

IMD incidence in PWH and non-PWH populations was calculated using National Center for Health Statistics' bridged-race postcensal population estimates [8] and the National Center for HIV/AIDS, Viral Hepatitis, STD, and TB

Published online 4 January 2024

Correspondence: Gabrielle Cooper, DrPH, MPH, 1600 Clifton Road NE, MS H24-8, Atlanta, GA 30329 (woz1@cdc.gov).

Open Forum Infectious Diseases®

https://doi.org/10.1093/ofid/ofad696

Prevention (NCHHSTP) AtlasPlus database [9]. HIV prevalence data from AtlasPlus were used to determine the PWH population size for each ABCs site. The non-PWH population denominator was calculated by subtracting the PWH population denominator from the census estimates for the ABCs catchment area. Denominator data were available for individuals aged ≥13 years in AtlasPlus, so all IMD incidence calculations were restricted to individuals aged ≥13 years. Proportions were calculated among those with known responses. Chi-square, Fisher exact, and Wilcoxon signed-rank tests were used to assess differences between IMD cases in PWH and non-PWH. Poisson regression was used to calculate relative risk estimates and 95% CIs. Data were analyzed using SAS, version 9.4.

This activity was reviewed by the CDC and was conducted consistent with applicable federal law and CDC policy (see e.g., 45 C.F.R. part 46.102(l)(2), 21 C.F.R. part 56; 42 U.S.C. §241(d); 5 U.S.C. §552a; 44 U.S.C. §3501 et seq). At each ABCs site, it was deemed either a public health assessment or human subjects research, for which approval was granted by local institutional review boards.

RESULTS

During 2009–2019, 636 IMD cases were reported within the ABCs surveillance area in individuals aged ≥13 years, with 16 (2.5%) of those cases occurring in PWH. There were no reported IMD cases in PWH aged <13 years. Among cases in PWH, patient sex was evenly distributed, and the median patient age was 46 years (Supplementary Table 1). The case-fatality ratio (CFR) was 18.8%, and bacteremia was found in 11 (68.8%) PWH cases. Of 15 PWH cases with known serogroup, 8 (53.3%) were serogroup C, 2 (13.3%) each were serogroup W, serogroup Y, and nongroupable, and 1 (6.7%) was serogroup B. No significant differences were observed between PWH and non-PWH aged ≥13 years when comparing age, sex, CFR, clinical syndrome, or serogroup.

Clinical data for the 16 cases in PWH showed that of those with known responses for each characteristic, 8 (57.1%) required intensive care unit admission, with 6 (37.5%) experiencing respiratory failure that required intubation (Table 1). Tobacco use was reported in 5 (31.3%) PWH. There was 1 PWH with asplenia and 1 with complement deficiency.

Most PWH had not received the MenACWY vaccine (n = 8 or 50%) or had an unknown vaccination history (n = 7 or 43.8%), with only 1 patient (6.3%) reporting previous MenACWY vaccination. Five (31.3%) of the 16 cases occurred after the 2016 ACIP recommendation for routine MenACWY vaccination in PWH. Of those 5 patients, 4 (80.0%) were unvaccinated, and 1 (20%) had an unknown vaccination history.

HIV-related clinical data showed that 8 (50.0%) PWH met the CDC AIDS surveillance case definition. Concurrent CD4 counts were available for 12 PWH, of whom 7 (58.3%) had CD4 counts <200 cells/μL. Five (50.0%) of the 10 PWH with available information on cART use reported current use of cART. More PWH meeting the AIDS surveillance case definition reported history of tobacco use and hepatitis C infection compared with PWH not meeting the AIDS surveillance case definition. All 3 deaths occurred in PWH with AIDS (Table 1).

The average annual incidence of IMD among PWH in the ABCs surveillance area during 2009–2019 was 6.2 (95% CI, 3.8–10.1) times higher than among non-PWH (0.96 vs 0.16 cases per 100 000). The annual IMD incidence among PWH ranged from 0 to 2.18 cases per 100 000 persons aged ≥13 years, compared with 0.11 to 0.28 cases per 100 000 among non-PWH persons aged ≥13 years. The IMD incidence among PWH in 2006–2016 was 0.95 cases per 100 000 persons aged ≥13 years, and incidence in 2017–2019 was 1.00 per 100 000 persons aged ≥13 years.

DISCUSSION

This study showed a sustained increased risk of IMD among PWH. Comparison of the incidence of IMD in PWH and non-PWH during 2009–2019 showed a statistically significant 6-fold higher IMD risk among PWH. The results of this analysis demonstrate that the current extent of increased risk among PWH in the United States remains comparable to that observed in prior studies [3–5]. However, the increase in risk we identified is lower than that in a previous CDC analysis in PWH meeting the AIDS surveillance case definition, which showed a 13-fold higher IMD risk [7]. The lower increase in risk observed among all PWH in our analysis may reflect the fact that our analysis focused on all PWH rather than exclusively patients meeting the AIDS surveillance case definition, who have greater immune impairment than other PWH, increasing their susceptibility to infectious diseases; however, the differences may also reflect the different time periods analyzed or stochastic differences due to small numbers. Additionally, the CDC surveillance case definition for HIV infection permanently classifies a person as Stage 3 AIDS, despite documented immune system recovery, and this classification may not represent current immunocompromised status in a patient on cART with well-controlled infection. Unfortunately, we were not able to calculate the increased risk specifically in people meeting the CDC AIDS surveillance case definition in the present study because appropriate denominator data for this calculation were not available.

The overall incidence of IMD is very low in the United States, so very few cases of IMD in PWH occur each year. The incidence of IMD in PWH may decline even further due to the 2016 ACIP recommendation for routine MenACWY vaccination for PWH; however, MenACWY vaccine uptake was low among PWH in this analysis. This finding is consistent with a

Table 1. Clinical Data for PWH With Invasive Meningococcal Disease Reported by Active Bacterial Core Surveillance Sites, 2009–2019 (n = 16)

Medical History, Physical Examination on Admission, and Complications		PWH With AIDS, No. (%)	PWH Without AIDS, No. (%)	Total, No. (%)
No.		8	8	16
History	Tobacco use	5 (62.5)	0	5 (31.3)
	Asplenia	1 (12.5)	0	1 (6.3)
	Complement deficiency	0	1 (12.5)	1 (6.3)
	Diabetes	1 (12.5)	1 (12.5)	2 (12.5)
	Hepatitis C infection	4 (50.0)	1 (12.5)	5 (31.3)
	Chronic renal disease	1 (12.5)	1 (12.5)	2 (12.5)
Previous meningococcal vaccination	Vaccinated	0	1 (12.5)	1 (6.3)
	Unvaccinated	4 (50.0)	4 (50.0)	8 (50.0)
	Unknown	4 (50.0)	3 (37.5)	7 (43.8)
Exam	Cachexia, malnourishment, or wasting	0	0	0
	Fever ≥100.5°F (38°C)	5 (83.3)	7 (87.5)	12 (85.7)
	Rash	1 (25.0)	2 (33.3)	3 (30.0)
	Altered mental status or comatose	4 (66.7)	5 (71.4)	9 (69.2)
Complications	ICU admission	4 (66.7)	4 (50.0)	8 (57.1)
	Respiratory failure requiring intubation	4 (50.0)	2 (25.0)	6 (37.5)
	Purpura fulminans	0	0	0
	Waterhouse-Friederichsen syndrome	0	0	0
Outcome				
	Survived	5 (62.5)	8 (100)	13 (81.3)
	Died	3 (37.5)	0	3 (18.8)
HIV-related clinical data[a]				
CDC AIDS surveillance case definition met		8 (100)	-	8 (50.0)
	History of AIDS-defining condition	3 (37.5)	-	3 (18.8)
	History of CD4 ever <200 cells/μL only	5 (62.5)	-	5 (31.3)
	Both AIDS-defining condition and CD4 criteria met	3 (37.5)	-	3 (18.8)
Concurrent CD4 count available		7 (87.5)	5 (62.5)	12 (75.0)
	≥500 cells/μL	0	1 (20.0)	1 (8.3)
	200–499 cells/μL	0	4 (80.0)	4 (33.3)
	<200 cells/μL	7 (100)	0	7 (58.3)
Reported cART use				
	Currently taking at time of presentation	2 (33.3)	3 (75.0)	5 (50.0)
	Previous use	3 (50.0)	0	3 (30.0)
	Never used	1 (16.7)	1 (25.0)	2 (20.0)
Currently taking opportunistic infection prophylaxis at time of presentation[b]		2 (28.6)	0	2 (13.3)

Percentages, shown in parentheses, were calculated based on the total with known information for each characteristic.

Abbreviations: cART, combination antiretroviral therapy; CDC, Centers for Disease Control and Prevention; ICU, intensive care unit.

[a]Reported data on CD4 percentages and HIV viral load testing were limited and are not shown.

[b]Defined as taking trimethoprim-sulfamethoxazole, azithromycin, dapsone, or other medication specifically for prophylaxis against *Pneumocystis* pneumonia or *Mycobacteriam avium* complex infection.

previous report that MenACWY vaccine uptake among PWH is low despite the 2016 ACIP recommendation of routine ACWY meningococcal vaccination for PWH [10]. In this prior report, only 16.3% of PWH received the MenACWY vaccine in the 2 years after their diagnosis. In addition, it is possible that some of the cases reported in our analysis were diagnosed with HIV at the time of their hospitalization for meningococcal disease. Such patients would not have had an opportunity to receive the recommended MenACWY vaccine before meningococcal disease onset, which may contribute to the low uptake observed.

Several limitations exist for this analysis. Due to the small number of IMD cases in PWH, the relative risk of IMD for PWH compared with non-PWH has wide confidence intervals, and comparison of characteristics of IMD cases in PWH with and without AIDS was not possible. Data on HIV viral loads, CD4 percentages, and CD4 count nadir history were limited, and we were therefore unable to describe these characteristics among our cases. Calculation of IMD incidence among PWH by demographic factors such as sex or age was not possible due to data suppression of denominators for these subpopulations in AtlasPlus to protect privacy. Additionally, persons with undiagnosed or unreported HIV infection may be misclassified in this analysis.

The 6-fold higher risk of IMD among PWH compared with non-PWH during 2009–2019 shows that PWH continue to

experience increased IMD risk. This result, combined with the low MenACWY vaccine coverage in this population reported previously, highlights the importance of improving implementation of the ACIP MenACWY vaccine recommendation for PWH, as well as the need for continued monitoring of IMD in PWH.

Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Acknowledgments

We thank the Active Bacterial Core surveillance system staff, including Kathy Angeles, Brenda Barnes, Lisa Butler, Kari Burzlaff, Kathryn Como-Sabetti, Melinda Eady, Catherine Lexau, Robert Mansmann, Tiffanie Markus, Carmen Marquez, Nancy Spina, Salina Torres, Lori Triden, and Daniel Wurm.

Financial support. This work was supported by a cooperative agreement with the Emerging Infections Program of the Centers for Disease Contol and Prevention (CDC-RFA-CK12-120205CONT16).

Disclaimer. The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the CDC.

Potential conflicts of interest. Lee H. Harrison reports reimbursement for travel to attend meetings for Merck, Pfizer, Sanofi, and GSK and participation on a Merck data safety monitoring board. Ruth Lynfield reports receiving payment for work as an associate editor for the American Academy of Pediatrics' (AAP) Red Book, which was donated to the Minnesota Department of Health, support from the Council of State and Territorial Epidemiologists for travel to meetings as president and vice president, travel support to ID Week by the Infectious Diseases Society of America, and support from AAP for travel to a committee meeting on infectious diseases in her role as associate editor. William Schaffner reports payment from the National Foundation for Infectious Disease for a leadership or fiduciary role. No other potential conflicts of interest were disclosed.

Patient consent. This study does not include factors necessitating patient consent.

References

1. Collin A, Le Marec FL, Vandenhende M-A, et al. Incidence and risk factors for severe bacterial infections in people living with HIV. ANRS CO3 Aquitaine Cohort, 2000-2012. PLoS One **2016;** 11:e0152970.
2. Harboe ZB, Larsen MV, Ladelund S, et al. Incidence and risk factors for invasive pneumococcal disease in HIV-infected and non-HIV-infected individuals before and after the introduction of combination antiretroviral therapy: persistent high risk among HIV-infected injecting drug users. Clin Infect Dis **2014;** 59:1168–76.
3. MacNeil JR, Rubin LG, Patton M, Ortega-Sanchez IR, Martin SW. Recommendations for use of meningococcal conjugate vaccines in HIV-infected persons – Advisory Committee on Immunization Practices, 2016. Morb Mortal Wkly Rep **2016;** 65:1189–94.
4. Folaranmi TA, Kretz CB, Kamiya H, et al. Increased risk for meningococcal disease among men who have sex with men in the United States, 2012–2015. Clin Infect Dis **2017;** 65:756–63.
5. Meiring S, Cohen C, de Gouveia L, et al. Declining incidence of invasive meningococcal disease in South Africa: 2003–2016. Clin Infect Dis **2019;** 69:495–504.
6. Selik RM, Mokotoff ED, Branson B, et al. Revised surveillance case definition for HIV infection—United States, 2014. MMWR Morb Mortal Wkly Rep **2014;** 63: 1–10.
7. Harris CM, Wu HM, Li J, Hall HI, Lee A, Zell E, et al. Meningococcal disease in patients with human immunodeficiency virus infection: a review of cases reported through active surveillance in the United States, 2000–2008. Open Forum Infect Dis **2016**; 3:ofw226.
8. National Center for Health Statistics. Bridged-race population estimates, United States. Available at: https://wonder.cdc.gov/bridged-race-population.html. Accessed 11 January 2024.
9. Centers for Disease Control and Prevention. NCHHSTP AtlasPlus. Updated **2019**. Available at: https://www.cdc.gov/nchhstp/atlas/index.htm. Accessed 11 January 2024.
10. Ghaswalla PK, Marshall GS, Bengtson LGS, Buikema AR, Bancroft T, et al. Meningococcal vaccination rates among people with a new diagnosis of HIV infection in the US. JAMA Netw Open **2022;** 5:e228573.