Open Forum Infectious Diseases

MAJOR ARTICLE

Risk Factors for Hospitalization and Effect of Immunosuppression on Clinical Outcomes Among an Urban Cohort of Patients With Mpox

William M. Garneau,[1] Joyce L. Jones,[2] Gabriella M. Dashler,[3] Heba H. Mostafa,[4] Seth D. Judson,[2] Nathan Kwon,[3] Matthew M. Hamill,[2] Elizabeth A. Gilliams,[2] David S. Rudolph,[3] Jeanne C. Keruly,[2] Amary Fall,[4] Eili Y. Klein,[3] Bhakti Hansoti,[3] and Kelly A. Gebo[2]

[1]Department of Medicine, Division of Hospital Medicine, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA, [2]Departent of Medicine, Division of Infectious Diseases, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA, [3]Department of Emergency Medicine, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA, and [4]Department of Pathology, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA

Background. During the 2022 mpox outbreak most patients were managed as outpatients, but some required hospitalization. Uncontrolled human immunodeficiency virus (HIV) has been identified as a risk factor for severe mpox.

Methods. Patients with mpox diagnosed or treated within the Johns Hopkins Health System between 1 June and 15 December 2022 were included. The primary outcome of interest was risk of hospitalization. Demographic features, comorbid conditions, treatment, and clinical outcomes were determined.

Results. A total of 353 patients were tested or treated for mpox; 100 had mpox diagnosed or treated (median age, 35.3 years; 97.0% male; 57.0% black and 10.0% Hispanic; 46.0% people with HIV [PWH]). Seventeen patients (17.0%) required hospitalization, 10 of whom were PWH. Age >40 years, race, ethnicity, HIV status, insurance status, and body mass index >30 (calculated as weight in kilograms divided by height in meters squared) were not associated with hospitalization. Eight of 9 patients (88.9%) with immunosuppression were hospitalized. Immunosuppression was associated with hospitalization in univariate (odds ratio, 69.3 [95% confidence interval, 7.8–619.7]) and adjusted analysis (adjusted odds ratio, 94.8 [8.5–1060.1]). Two patients (11.8%) who were hospitalized required intensive care unit admission and died; both had uncontrolled HIV infection and CD4 T-cell counts <50/μL. Median cycle threshold values for the first positive mpox virus sample did not differ between those who were hospitalized and those who were not.

Conclusions. Immunosuppression was a significant risk factor for hospitalization with mpox. PWH with CD4 T-cell counts <50/μL are at high risk of death due to mpox infection. Patients who are immunosuppressed should be considered for early and aggressive treatment of mpox, given the increased risk of hospitalization.

Keywords. antiviral agents; clinical outcomes; HIV/AIDS; Monkeypox virus; Mpox.

Mpox is a zoonotic disease caused by the mpox virus (MPXV), an orthopoxvirus, endemic in parts of West and Central Africa, that has caused limited outbreaks throughout the world since its identification in 1958 [1]. In 2022, a sharp rise in mpox cases caused by the MPXV, including reports in multiple nonendemic countries, led the World Health Organization to formally declare a public health emergency on 23 July 2022 [2].

As of September 2023, >90 000 cases worldwide and >30 000 in the United States have been identified [2, 3]. The virus was previously divided into clade I (formerly West African) and clade II (formerly Congo Basin) [4]. Initial reports in the summer of 2022 noted that most infections were clade II and occurred in men who have sex with men and people with human immunodeficiency virus (HIV) (PWH) [4–7]. Early mitigation efforts in the United States were focused on increased surveillance capacity, prevention methods such as the JYNNEOS vaccine, which received emergency use authorization on 8 August 2022, and public health information campaigns targeted to providers and the general public [8].

For patients with a diagnosis of mpox, there is no Food and Drug Administration–approved treatment; however, multiple agents—including tecovirimat, cidofovir, brincidofovir, and vaccinia immune globulin—were used by clinicians in patients at risk of severe disease [9, 10]. While the majority who contracted mpox were treated conservatively, some patients developed severe symptoms and required hospitalization. There are limited published accounts of patients with severe disease, describing the characteristics and outcomes in this group of patients [7, 11, 12]. The current study was designed to evaluate risk factors

Received 23 August 2023; editorial decision 17 October 2023; accepted 30 October 2023; published online 5 December 2023

Correspondence: William M. Garneau, MD MPH, Department of Medicine, Division of Hospital Medicine, Johns Hopkins University School of Medicine, 600 N Wolfe St, Carnegie 2nd Floor, Ste 249, Baltimore, MD 21287 (william.garneau@jhmi.edu).

Open Forum Infectious Diseases®

https://doi.org/10.1093/ofid/ofad533

for hospitalizations and outcomes of patients with mpox within a large, urban multisite hospital system and to assess MPXV cycle threshold (Ct) values among available viral samples.

METHODS

We abstracted data from the Johns Hopkins Infectious Diseases Precision Medicine Center of Excellence (IDPMCOE) registry, a database that includes both inpatient and outpatient electronic medical records (EMRs) for patients with an infectious disease diagnosed within the Johns Hopkins Health System (JHHS). The JHHS includes >40 outpatient facilities and 6 hospitals in Maryland, Florida, and Washington, DC. Patients tested for mpox within the JHHS from 1 June to 15 December 2022 were included in the study. A query was performed on the IDPMCOE registry to identify patients who underwent testing and treatment for mpox at JHHS. In addition to those identified via query, patients with mpox diagnosed at Johns Hopkins Sibley Memorial Hospital were identified and added, as MPXV testing was processed through the Washington, DC Department of Health and not JHHS, per protocol at the time. Records were manually reviewed to confirm the diagnosis, and additional clinical information was obtained through record review by study team members (W. M. G., J. L. J., G. M. D., S. D. J., E. A. G., D. S. R., and J. C. K.).

Patient characteristics—including age at mpox diagnosis, sex at birth, insurance status, self-reported race, and ethnicity—were downloaded from the IDPMCOE. Gender identity, HIV risk factor, sexually transmitted infection testing, reason for admission, treatment type, length of stay, surgical consultation, highest level of inpatient care, and outcome of hospitalization were manually abstracted (Research Electronic Data Capture [REDCap], version 13.1.33; Vanderbilt University) [13, 14]. Pregnancy status and comorbid conditions (including hypertension, body mass index >30 (calculated as weight in kilograms divided by height in meters squared), diabetes mellitus, and HIV infection) were recorded from the EMR. Immunocompromised status was defined according to the Centers for Disease Control's interim [10] clinical guidance for treating mpox: poorly controlled HIV (CD4 T-cell count <200/μL or detectable HIV-1), cancer, solid organ transplant, receipt of stem-cell transplant, autoimmune disease with immunodeficiency, or receipt of immunocompromising medication (Supplementary Appendix).

Treatment for mpox was manually abstracted from the EMR. For PWH, records were abstracted for receipt of antiretroviral therapy (ART) and CD4 T-cell count and HIV-1 RNA closest to the time of mpox diagnosis. Inpatient treatment was defined as any hospitalization for mpox diagnosis. Outpatient treatment included clinic and emergency department visits. Records were reviewed to identify reasons for admission among those hospitalized. Vaccine status for JYNNEOS or ACAM2000 was recorded as vaccinated, unvaccinated or unknown. Vaccination was defined as record documentation of receipt of 2 doses of vaccine 2 weeks before clinical presentation. Logistic regression was used to assess the impact of demographic and clinical characteristics associated with hospitalization using Stata software [15]. The first positive sample, obtained at admission, with valid internal control and Ct value <30 was included for analysis. Viral typing and Ct values of the diagnostic orthopoxvirus polymerase chain reaction results were obtained from samples [16, 17]. Median Ct values were compared between hospitalized and nonhospitalized patients using Kruskal-Wallis test.

The design of the work was approved by the Johns Hopkins Institutional Review Board under a waiver of informed consent, given the observational nature of the work and use of deidentified data (IRB00347138). The work was carried out in accordance with institutional privacy policies, and data were analyzed and stored within a prespecified protected environment.

RESULTS

A total of 340 patients were identified as having received testing or treatment at JHHS. In addition, 13 patients were identified by the Washington, DC, Health Department who carried out confirmatory testing for patients at Sibley Memorial Hospital per local testing policy at the time. Of the patients identified, 37 patients were excluded because they were <18 years of age, and 216 tested negative; 100 patients received a diagnosis of and/or received care for mpox in the JHHS between 1 June and 15 December 2022 and were included in this analysis (Figure 1). Most patients were male (97.0%) and black (57.0%); the median age (range) was 35.3 (19.0–65.6) years, and nearly half were PWH (46.0%) (Table 1). A minority were Hispanic (10.0%). Of the 100 patients with mpox, 83 (83.0%) were treated as outpatients, and 17 (17.0%) required hospitalization. Nine patients were documented as receiving JYNNEOS vaccination during the inclusion period, but none had completed the series 2 weeks before mpox diagnosis.

Nearly 1 in 5 patients who were treated as outpatients received oral tecovirimat (16.9%), and 14 of 17 (82.4%) who were hospitalized received mpox-specific therapy. The only specific therapy used for outpatients was oral tecovirimat (16.9%). The most common therapy for inpatients was oral tecovirimat (82.4%), and then intravenous tecovirimat (23.5%). In addition, 11.8% received vaccinia immune globulin, 11.8% received cidofovir, and 11.8% received trifluridine eye drops (Table 2). Of the 3 patients who were admitted with mpox but not treated with antiviral therapy, 2 required pain control, and 1 was admitted in the context of possible procedural intervention.

There was no difference in the odds of hospitalization by age, race, ethnicity, HIV status, insurance status, or body mass

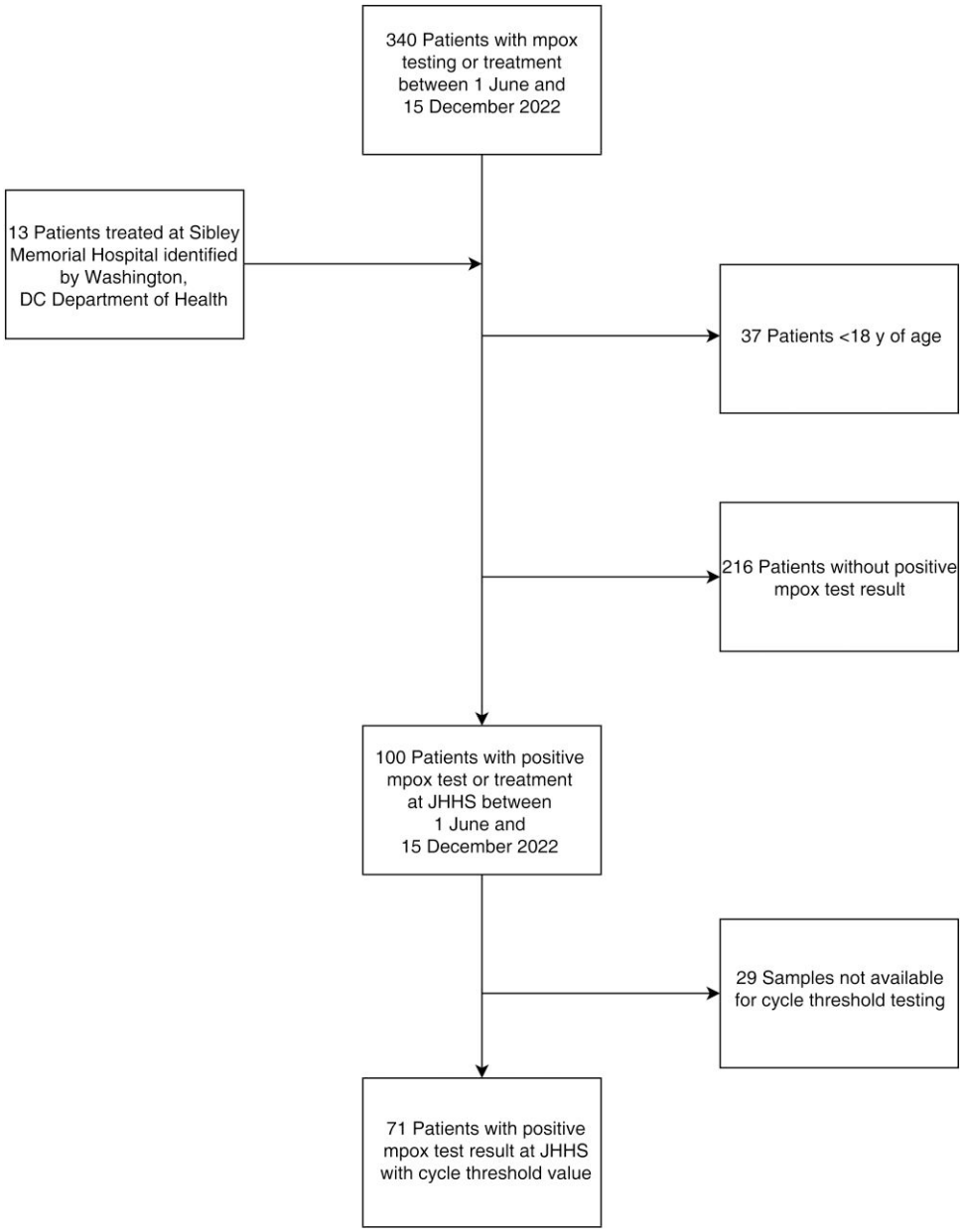

Figure 1. Patients evaluated for mpox at the Johns Hopkins Health System (JHHS) from 1 June to 15 December 2022.

index (Table 3). Eight of the 9 patients (88.9%) who were immunosuppressed required hospitalization (Table 4). Immunosuppression was associated with hospitalization in univariate (odds ratio, 69.3 [95% confidence interval, 7.8–619.7]) and multivariate (adjusted odds ratio, 94.8 [8.5–1060.1]) analysis (Table 3).

Patients could be hospitalized for multiple causes, and the most common reason for admission was pain control (82.4%) followed by bacterial superinfection (29.4%), urethritis (17.6%), need for isolation (17.6%), and inability to swallow (11.8%). No patients were hospitalized solely for isolation or for confirmatory testing. Among hospitalized patients, 3 (17.6%) had syphilis, 1 had herpes simplex (5.9%), and 1 (5.9%) had chlamydia diagnosed concomitantly. The median length of stay (range) was 4 (1–55) days. More than a third of patients required surgical consultation during hospitalization (35.3%), and 11.8% of hospitalized patients required intensive care unit (ICU) admission. The median length of stay (range) among patients requiring ICU admission was 52 (49–55) days. The 2 patients who died of mpox were men with advanced HIV/AIDS and CD4 T-cell counts <50/μL, and they were not on ART at the time of diagnosis. Both were hospitalized after

Table 1. Baseline Characteristics of Patients With an Mpox Diagnosis

Characteristic	Patients, No. (%)[a]		
	All Patients (n = 100)	Not Admitted (n = 83)	Admitted to Hospital (n = 17)
Age, median (range), y	35.3 (19.0–65.6)	34.3 (19.0–65.6)	38.8 (25.3–56.8)
Sex			
Male	97 (97.0)	81 (97.6)	16 (94.1)
Female	3 (3.0)	2 (2.4)	1 (5.9)
Gender			
Male	94 (94.0)	79 (95.2)	15 (88.2)
Female	3 (3.0)	2 (2.4)	1 (5.9)
Transgender female	3 (3.0)	2 (2.4)	1 (5.9)
Transgender male	0 (0)	0 (0)	0 (0)
Race			
Black or African American	57 (57.0)	46 (55.4)	11 (64.7)
White	27 (27.0)	22 (26.5)	5 (29.4)
Asian	2 (2.0)	2 (2.4)	0 (0)
American Indian or Alaska Native	1 (1.0)	1 (1.2)	0 (0)
Other	12 (12.0)	11 (13.3)	1 (5.9)
Choose not to disclose	1 (1.0)	1 (1.2)	0 (0)
Ethnicity			
Hispanic/Latino	10 (10.0)	8 (9.6)	2 (11.8)
Not Hispanic or Latino	89 (89.0)	74 (89.2)	15 (88.2)
Unknown	1(1.0)	1 (1.2)	0 (0)
Sexual orientation			
Gay	64 (64)	51 (61.4)	13 (76.5)
Bisexual	14 (14)	13 (15.7)	1 (5.9)
Straight (not lesbian or gay)	11 (11)	8 (9.6)	3 (17.6)
Unknown	11 (11)	11 (13.3)	0 (0)
Injection drug use			
Yes	2 (2.0)	1 (1.3)	1 (5.9)
No	91 (91.0)	76 (91.6)	15 (88.2)
Unknown	7 (7.0)	6 (7.2)	1 (5.9)
Comorbid condition			
HTN	10 (10.0)	7 (8.4)	3(17.6)
BMI >30[b]	16 (16.0)	11 (13.3)	5 (29.4)
Diabetes mellitus	4 (4.0)	3 (3.6)	1 (5.9)
HIV infection	46 (46.0)	36 (43.4)	10 (58.8)
None	20 (20.0)	19 (22.9)	1 (5.9)
Unknown	2 (2.0)	2 (2.4)	0 (0)
Immunosuppression			
Yes	9 (9.0)	1 (1.2)	8 (47.1)
No	87 (87.0)	78 (94.0)	9 (52.9)
Unknown	4 (4.0)	4 (4.8)	0 (0)
Insurance status			
Medicaid	35 (35.0)	29 (34.9)	6 (35.3)
Medicare	2 (2.0)	1 (1.2)	1 (5.9)
Private insurance	52 (52.0)	44 (53.0)	8 (47.1)
Uninsured	6 (6.0)	4 (4.8)	2 (11.8)
Unknown	5 (5.0)	5 (6.0)	0 (0)

Abbreviations: BMI, body mass index; HIV, human immunodeficiency virus; HTN, hypertension.

[a]Data represent no. (%) of patients unless otherwise specified.

[b]BMI calculated as weight in kilograms divided by height in meters squared.

treatment with tecovirimat. Ultimately, their conditions deteriorated despite initiation of ART, additional courses of tecovirimat, intravenous vaccinia immune globulin, and courses of cidofovir. Both patients required ICU admission owing to diffuse necrotic wounds needing debridement, complicated by bacteremia and multisystem organ failure and ultimately leading to death (Table 5).

Of the 100 patients included in analysis of mpox outcomes at JHHS during the study period, 71 patients (71.0%) with mpox had Ct values were included in the analysis. Patients whose

Table 2. Treatment for Mpox and for Complications Stratified by Patients' Hospital Admission Status

Treatment	Patients, No. (%)	
	Not Admitted (n = 83)	Admitted (n = 17)
Mpox-specific treatment		
Tecovirimat (oral)	14 (16.9)	14 (82.4)
Tecovirimat (intravenous)	0 (0)	4 (23.5)
Vaccinia immune globulin	0 (0)	2 (11.8)
Cidofovir	0 (0)	2 (11.8)
Trifluridine eye drops	0 (0)	2 (11.8)
Treatment for complications		
Antibiotics	20 (24.1)	13 (76.5)
Opiate pain control	4 (4.8)	13 (76.5)
None	51 (61.4)	0 (0)

Table 3. Risks of Hospitalization in Univariate and Multivariate Analyses (N = 100)

Factor	OR (95% CI)	
	Univariate Analysis	Multivariate Analysis
Age >40 vs ≤40 y[a]	2.1 (0.7–6.0)	2.8 (0.7–11.2)
Black vs nonblack	1.4 (0.5–4.3)	…
Hispanic vs non-Hispanic	1.2 (0.2–6.4)	…
MSM vs non-MSM	1.5 (0.4–5.7)	…
Uninsured vs other insurance status[a]	2.5 (0.4–14.7)	0.5 (0.03–8.6)
BMI >30 vs ≤30[b]	2.7 (0.8–9.0)	…
Living with vs not living with HIV	1.8 (0.6–5.2)	…
Immunosuppressed vs not immunosuppressed[a]	69.3 (7.8–619.7)	94.8 (8.5–1060.1)

Abbreviations: BMI, body mass index; CI, confidence interval; HIV, human immunodeficiency virus; MSM, men who have sex with men; OR odds ratio.

[a]Factors included in the multivariate analysis.

[b]BMI calculated as weight in kilograms divided by height in meters squared.

samples were not included were those with mpox diagnosed at a non-JHHS laboratory or for whom a sample was not available (n = 27) or was obtained after initial diagnosis (n = 2). All samples with virologic data were clade II. Of the 71 samples with Ct values, there was no difference between median Ct values in hospitalized patients (median Ct [range], 18.4 [16.1–23.3]) and those treated as outpatients (median Ct, 18.4; 15.1–37.0) ($P = 0.7$).

DISCUSSION

This study has several important findings. First, a significant percentage of patients with mpox required hospitalization. Second, immunocompromised patients were at a higher risk of hospitalization as well as death.

The hospitalization rate of 17.0% in our study is slightly higher than in contemporaneous reports [5, 18, 19]. An *MMWR* report from May–July 2022 in the United States recorded a 8.1% hospitalization rate for mpox among a similar proportion of PWH (41%) [5], but the reason for admission was not captured. A case series of 197 participants with mpox diagnosed in 2022 in London found a hospitalization rate of 10.2% for patients with clinical reasons for admission (10.2%) and a higher rate of hospitalization when those hospitalized for isolation were included (12.7%) [18]. The latter hospitalization rate is similar to that in a global case series of 528 people with mpox, which demonstrated a hospitalization rate of 13% [19]. We report a higher rate of hospitalization, which may be accounted for by the inclusion of a tertiary care center with a wide catchment area for referral and more acute illness overall. In line with other authors, we found a similarly high rate of intercurrent sexually transmitted infection: 17.6% of hospitalized patients in the current study had syphilis diagnosed, consistent with findings in the London cohort [18] (21.1% positive for *Neisseria gonorrhoeae*) and the global case series (29% positive for a concomitant sexually transmitted infection) [19].

Our study is also notable for the increased risk of hospitalization in immunocompromised patients. Prior studies have highlighted the risk of severe mpox among PWH with CD4 T-cell counts <350/μL, supporting the likelihood that increased mpox morbidity in PWH is related to immunosuppression. Consistent with findings in the global case series of 382 cases of mpox among PWH with CD4 T-cell counts <350/μL, reported by Mitjà et al [20], we also noted an increased hospitalization rate with decreasing CD4 T-cell counts. Our findings suggest that the risk of severe mpox is not limited to persons with HIV with decreased CD4 T-cell counts but includes other forms of immunodeficiency. A recent study analyzing outcomes of tecovirimat treatment for patients with diagnosed mpox who were stratified by HIV status did not find an elevated hospitalization rate in the PWH cohort; however, that study did not include conditions other than HIV and included only 4 PWH with a CD4 T-cell count <200/μL [21].

Among 100 patients with mpox diagnosis in our study, 2 died, for a case fatality rate of 2.0%. This is significantly higher than the 0.3% reported mortality rate in the meta-analysis of 19 mpox studies, including both clade I and clade II infections; however rates, appear to depend on clade and era [22]. Our findings suggest a significant mortality rate associated with immunosuppression and mpox clade II. This is supported by a recent *MMWR* report of 38 deaths due to mpox infection—93.9% of patients with complete data were PWH, and 95.8% had CD4 T-cell counts <50/μL [23]. Our study further highlights the challenge of delayed initiation of ART and immune reconstitution inflammatory syndrome in the setting of treating patients with advanced HIV and severe mpox infection, which has been noted previously [20].

We found that the initial Ct values of mpox specimens were not correlated with the need for hospitalization. However, these

Table 4. Characteristics and Outcomes in Patients With Immunosuppression

Decade of Age	Immunosupressing Condition	CD4 T-Cell Count, Cells/μL	HIV-1 RNA, Copies/mL	Ct Value	Tecovirimat Treatment	Outcome
21–30 y	Poorly controlled HIV	<50	>10 000	NA	Yes	Hospitalization
	Poorly controlled HIV	200–499	2000–10 000	17.04	Yes	Hospitalization
31–40 y	Poorly controlled HIV	200–499	<50	21.02	Yes	Hospitalization
	Solid organ transplant, HIV	>500	<50	16.1	Yes	Hospitalization
	Cancer, chemotherapy, HIV	>500	<50	NA	No	Outpatient treatment
	Poorly controlled HIV	50–199	>10 000	NA	Yes	Hospitalization
41–50	Poorly controlled HIV	<50	>10 000	NA	Yes	Death
	Poorly controlled HIV	<50	2000–10 000	NA	Yes	Death
51–60	ESRD, MGUS	NA	NA	18.35	Yes	Hospitalization

Abbreviations: Ct value, cycle threshold value; ESRD, end-stage renal disease; HIV, human immunodeficiency virus; MGUS, monoclonal gammopathy of undetermined significance; NA, not available.

Table 5. Characteristics of Hospitalizations in Patients Hospitalized for Mpox

Characteristic	Patients, No. (%)[a] (n = 17)
Reasons for admission[b]	
Pain control	14 (82.4)
Bacterial superinfection	5 (29.4)
Urethritis	3 (17.6)
Need for isolation	3 (17.6)
Unable to swallow	2 (11.8)
Length of stay, median (range), d	4 (1–55)
Sexually transmitted infection[b]	
None	12 (70.6)
Syphilis	3 (17.6)
Chlamydia	1 (5.9)
Herpes simplex	1 (5.9)
Surgical consultation during admission	6 (35.3)
Type of subspecialty consultation[b]	
Ophthalmology	2 (11.8)
Urology	2 (11.8)
Gastroenterology	2 (11.8)
Plastic surgery	2 (11.8)
ICU admission	2 (11.8)
Length of stay for patients requiring ICU-level care, mean, d	52
Death during hospitalization	2 (11.8)

Abbreviation: ICU, intensive care unit.

[a]Data represent no. (%) of patients unless otherwise specified.

[b]Including all that apply.

findings should be interpreted with caution, as we were able to include only 71 of 100 patients in our analysis of Ct values. Future larger studies should further explore the impact of Ct on mpox outcomes. In addition, Ct values are dependent on the technique used to obtain samples, the time from symptom onset, and the sample source, which were not explored in this analysis [24, 25].

The current study has several important limitations. First, it is small and includes only 17 patients with the outcome of interest, limiting our ability to perform multivariate analysis. The study catchment includes a single large urban health center in the United States with a tertiary referral network. It may also underestimate of the total number of cases within the system, as some persons with self-limited cases may not have presented to medical attention or may have been seen outside our hospital system. None of the patients in our study had received JYNNEOS vaccination 2 weeks before diagnosis, so the effect of vaccination on outcomes is not clear. In addition, while we can confirm receipt of outpatient prescription for tecovirimat, we were not able to determine adherence to therapy. Assessment of clinical outcome was done by record review of available medical records. It is possible that patients sought care at facilities beyond ours after diagnosis.

In summary, we demonstrate increased risks of hospitalization and disease severity due to mpox in persons with immune suppression. In addition to advanced HIV, other immunocompromising conditions, such as solid organ transplant, were associated with more severe mpox infection. Future larger studies focused on the prevention of mpox and the effects of vaccination and early antiviral therapy on clinical outcomes are essential, given the heightened risk in this subpopulation.

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.

Notes

Acknowledgments. The authors gratefully acknowledge the study participants who generously gave of their time and provided biological specimens and the passionate study personnel who facilitated these studies.

Author contributions. Substantial contributions to the conception or design of the work: W. M. G., J. L. J., B. H., and K. A. G. Substantial contributions to the acquisition or analysis of data for the work: All authors. Substantial contributions to the interpretation of data for the work: W. M. G., J. L. J., B. H., and K. A. G. Drafting the work or revising it critically for important intellectual content: W. M. G., J. L. J., and K. A. G.

Senior author: K. A. G. Final approval of the version to be published: All authors. Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved: W. M. G.

Disclaimer. The study sponsors did not contribute to the study design, the collection, analysis, and interpretation of data, or the decision to submit this manuscript for publication. The content is solely the responsibility of the authors and does not necessarily represent the official views of the funders.

Financial support. This work was supported by the Johns Hopkins University Center for AIDS Research (grant P30AI094189), the National Institutes of Health National Center for Advancing Translational Sciences (grant KL2TR003099), the Johns Hopkins University Clinical Characterization Protocol for Severe Emerging Infections grant and the US Centers for Disease Control and Prevention (grant U01CK000589 to E. Y. K.).

Potential conflicts of interest. W. M. G reports receiving a honorarium from DKBmed; serving as a scientific advisor to Gilead Sciences; and owning stock in Abbott Laboratories, Danaher, Eli Lilly, Iqvia, Johnson & Johnson, Stryker, UnitedHealth Group, and AstraZeneca Pharmaceuticals. K. A. G. reports payment from the Aspen Institute, Teach For America, Premier, and UpToDate and reports a nonpaid position on the scientific advisory board for Pfizer. All other authors report no potential conflicts.

References

1. Lum FM, Torres-Ruesta A, Tay MZ, et al. Monkeypox: disease epidemiology, host immunity and clinical interventions. Nat Rev Immunol **2022**; 22:597–613.
2. World Health Organization. WHO director-general's statement at the press conference following IHR emergency committee regarding the multi-country outbreak of monkeypox—23 July 2022. Published 2022. Available at: https://www.who.int/director-general/speeches/detail/who-director-general-s-statement-on-the-press-conference-following-IHR-emergency-committee-regarding-the-multi–country-outbreak-of-monkeypox–23-july-2022. Accessed 26 June 2023.
3. Centers for Disease Control and Prevention. 2022 Outbreak cases and data. Published 19 July 2023. Available at: https://www.cdc.gov/poxvirus/mpox/response/2022/index.html. Accessed 30 September 2023.
4. Gigante CM, Korber B, Seabolt MH, et al. Multiple lineages of monkeypox virus detected in the United States, 2021–2022. Science **2022**; 378:560–5.
5. Philpott D, Hughes CM, Alroy KA, et al. Epidemiologic and clinical characteristics of monkeypox cases—United States, May 17–July 22, 2022. MMWR Morb Mortal Wkly Rep **2022**; 71:1018–22.
6. Tarín-Vicente EJ, Alemany A, Agud-Dios M, et al. Clinical presentation and virological assessment of confirmed human monkeypox virus cases in Spain: a prospective observational cohort study. Lancet **2022**; 400:661–9.
7. Miller MJ, Cash-Goldwasser S, Marx GE, et al. Severe monkeypox in hospitalized patients—United States, August 10–October 10, 2022. MMWR Morb Mortal Wkly Rep **2022**; 71:1412–7.
8. Kava CM, Rohraff DM, Wallace B, et al. Epidemiologic features of the monkeypox outbreak and the public health response—United States, May 17–October 6, 2022. MMWR Morb Mortal Wkly Rep **2022**; 71:1449–56.
9. Centers for Disease Control and Prevention. Expanded access IND protocol: use of tecovirimat (TPOXX®) for treatment of human non-variola orthopoxvirus infections in adults and children. **2023**. Available at: https://www.cdc.gov/poxvirus/mpox/pdf/Tecovirimat-IND-Protocol-CDC-IRB.pdf. Accessed 21 July 2023.
10. Centers for Disease Control and Prevention. Treatment information for healthcare professionals. Published 10 July 2023. Available at: https://www.cdc.gov/poxvirus/mpox/clinicians/treatment.html. Accessed 21 July 2023.
11. Govind A, Lazarte SM, Kitchell E, et al. Severe mpox infections in people with uncontrolled human immunodeficiency virus. Clin Infect Dis **2023**; 76:1843–6.
12. Hermanussen L, Brehm TT, Wolf T, et al. Tecovirimat for the treatment of severe mpox in Germany. Infection **2023**; 51:1563–8.
13. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research Electronic Data Capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform **2009**; 42:377–81.
14. Harris PA, Taylor R, Minor BL, et al. The REDCap consortium: building an international community of software platform partners. J Biomed Inform **2019**; 95: 103208.
15. StataCorp. Stata Statistical Software. Published 2023. https://www.stata.com/support/faqs/resources/citing-software-documentation-faqs/
16. Uhteg K, Mostafa HH. Validation and implementation of an orthopoxvirus qualitative real-time PCR for the diagnosis of monkeypox in the clinical laboratory. J Clin Virol **2023**; 158:105327.
17. Li Y, Zhao H, Wilkins K, Hughes C, Damon IK. Real-time PCR assays for the specific detection of monkeypox virus West African and Congo basin strain DNA. J Virol Methods **2010**; 169:223–7.
18. Patel A, Bilinska J, Tam JCH, et al. Clinical features and novel presentations of human monkeypox in a central London centre during the 2022 outbreak: descriptive case series. BMJ **2022**; 378:e072410.
19. Thornhill JP, Barkati S, Walmsley S, et al. Monkeypox virus infection in humans across 16 countries—April–June 2022. N Engl J Med **2022**; 387:679–91.
20. Mitjà O, Alemany A, Marks M, et al. Mpox in people with advanced HIV infection: a global case series. Lancet Lond Engl **2023**; 401:939–49.
21. McLean J, Stoeckle K, Huang S, et al. Tecovirimat treatment of people with HIV during the 2022 mpox outbreak : a retrospective cohort study. Ann Intern Med **2023**; 176:642–8.
22. DeWitt ME, Polk C, Williamson J, et al. Global monkeypox case hospitalisation rates: a rapid systematic review and meta-analysis. eClinicalMedicine **2022**; 54: 101710.
23. McQuiston JH, Braden CR, Bowen MD, et al. The CDC domestic mpox response—United States, 2022–2023. MMWR Morb Mortal Wkly Rep **2023**; 72:547–52.
24. Martins-Filho PR, Tanajura DM, Alves Dos Santos C. Polymerase chain reaction positivity and cycle threshold values in biological samples from patients with monkeypox: a meta-analysis. Travel Med Infect Dis **2022**; 50:102448.
25. Edman-Wallér J, Jonsson O, Backlund G, Muradrasoli S, Sondén K. Results of PCR analysis of mpox clinical samples, Sweden, 2022. Emerg Infect Dis **2023**; 29:1220–2.