

## CLINICAL AND EPIDEMIOLOGICAL CHARACTERISTICS OF THE 2022-2023 MPOX OUTBREAK IN BUENOS AIRES, ARGENTINA

ROMINA MAUAS<sup>1</sup>, MARÍA JOSÉ ROLÓN<sup>2</sup>, FABIANA MONTALDO<sup>2</sup>, GUSTAVO LOPARDO<sup>3</sup>, AGUSTINA FIORI<sup>3</sup>,  
ÁNGELES TISNÉ<sup>4</sup>, ELENA OBIETA<sup>5</sup>, SOFÍA PELAEZ<sup>5</sup>, ROSANA CUINI<sup>6</sup>, VERÓNICA CACCIARI<sup>6</sup>, MARÍA MARTA GRECO<sup>7</sup>,  
GASTÓN COPERTARI<sup>1,8</sup>, LILIANA CALANNI<sup>9</sup>, PABLO PARENTI<sup>10</sup>, GUSTAVO CASTRO<sup>1</sup>, ANABELLA ERVITI<sup>1</sup>,  
MARTÍN BRIZUELA<sup>1</sup>, MARÍA FERNANDA ROMBINI<sup>1</sup>, EDGARDO BOTTARO<sup>1</sup>, DIEGO CECCHINI<sup>1,4</sup>, ISABEL CASSETTI<sup>1,3</sup>

<sup>1</sup>Helios Salud, Buenos Aires, <sup>2</sup>Hospital General de Agudos Dr. Juan A. Fernández, Buenos Aires, <sup>3</sup>Centro de Estudios Infectológicos Dr. Stambouljian, Buenos Aires, <sup>4</sup>Hospital General de Agudos Dr. Cosme Argerich, Buenos Aires, <sup>5</sup>Hospital Municipal Ciudad de Boulogne, Buenos Aires, <sup>6</sup>Hospital General de Agudos Dr. Teodoro Álvarez, Buenos Aires, <sup>7</sup>Hospital Español de La Plata, Buenos Aires, <sup>8</sup>Hospital Municipal Prof. Dr. Bernardo A. Houssay, Buenos Aires, <sup>9</sup>Unidad Infectológica Neuquén (CEIN), Neuquén, <sup>10</sup>Universidad Nacional de Rosario, Santa Fe, Argentina

**Postal address** Diego Cecchini, Helios Salud SA, Perú 1511/15, 1141 Buenos Aires, Argentina

**E-mail:** dcecchini@heliossalud.com.ar

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### Abstract

**Introduction:** The 2022-2023 Mpox outbreak in Argentina presented unique challenges due to the lack of vaccination and antiviral therapy. This study analyzed the epidemiological and clinical characteristics of cases in the Buenos Aires Metropolitan Area (MABA), examining temporal trends, HIV status, and concomitant sexually transmitted infections (STIs).

**Materials and methods:** An ambispective, analytic, and multicenter study was conducted between September 2022 and May 2023 in HIV/STI clinics and hospitals in MABA. Cases were classified as confirmed (positive PCR) or possible (clinical and epidemiological criteria). Patients infected with Mpox with and without HIV were compared.

**Results:** 247 patients were included, 95.5% were confirmed cases. The median age was 36 years; 98% were men; 93.7% were men who have sex with men. Sexual exposure was the main transmission route (91%). The 25.2% presented concomitant STIs. The 74% were people living with HIV (PLWH), with good immuno-virological control. Common clinical manifestations included papular, pustular, and vesicular lesions; 59.4% presented >20 lesions. Rectal involvement occurred in 25.6%. Complications were observed in 9.3%, hospitalization in 6.6%, and mortality was 0.4%. PLWH showed a higher prevalence of perianal lesions and proctitis, without differences in complications and hospitalization.

**Discussion:** The outbreak in Argentina, mainly affecting men who have sex with men living with HIV, had low mortality. No significant differences were observed in complications and hospitalization between people with and without HIV.

**Key words:** Mpox, Argentina, mortality, complications

### Resumen

*Características clínicas y epidemiológicas del brote de Mpox en Buenos Aires, Argentina, 2022-23*

**Introducción:** El brote de Mpox en Argentina 2022-2023, presentó desafíos únicos debido a la falta de vacunación y terapia antiviral. Este estudio analizó las características epidemiológicas y clínicas de los casos en el Área Metropolitana de Buenos Aires (AMBA), examinando tendencias temporales, estatus para HIV e infecciones de transmisión sexual (ITS) concomitantes.

**Materiales y métodos:** Se realizó un estudio ambispectivo, analítico y multicéntrico entre septiembre 2022 y mayo 2023 en clínicas de HIV/ITS y hospitales del AMBA. Los casos se clasificaron como confirmados (PCR positiva) o posibles (criterios clínicos y epidemiológicos). Se compararon los pacientes infectados con Mpox con y sin HIV.

**Resultados:** Se incluyeron 247 pacientes, 95.5% fueron casos confirmados. La edad mediana fue 36 años; 98% hombres; 93.7% hombres que tienen sexo con hombres. La exposición sexual fue la principal ruta de transmisión (91%). El 25.2% presentó ITS concomitantes. El 74% eran personas viviendo con HIV (PVHIV), con buen control inmuno-virológico. Las manifestaciones clínicas comunes incluyeron lesiones papulares, pustulares y vesiculares; el 59.4% presentó >20 lesiones. La afectación rectal ocurrió en el 25.6%. Se observaron complicaciones en el 9.3%, hospitalización en el 6.6%, y una mortalidad del 0.4%. Las PVHIV mostraron mayor prevalencia de lesiones perianales y proctitis, sin diferencias en complicaciones y hospitalización.

**Discusión:** El brote de Mpox en Argentina en 2022-2023, afectó principalmente a hombres que tienen sexo con hombres viviendo con HIV y presentó baja mortalidad. No se observaron diferencias significativas en complicaciones y hospitalización entre personas con y sin HIV.

**Palabras clave:** Mpox, Argentina, mortalidad, complicaciones

## KEY POINTS

### Current knowledge

- Mpox outbreaks in non-endemic areas primarily affected men who have sex with men. People living with HIV (PLWH) were disproportionately impacted. Limited data existed on Mpox in Latin America, especially regarding clinical presentation and outcomes in PLWH versus HIV-negative individuals.

### Contribution of the article to current knowledge:

- This study characterizes the Mpox outbreak in Buenos Aires Metropolitan Area, Argentina, where vaccination was unavailable. It reveals similar clinical presentations and outcomes in PLWH and HIV-negative individuals, with good immunological status in most PLWH. Complications were associated with CD4+ counts <350 cells/mL. The outbreak self-limited despite lack of vaccination, raising questions about population susceptibility to future outbreaks.

Monkeypox is a zoonotic disease endemic to Central and Western Africa caused by a virus of the genus *Orthopoxvirus*, family *Poxviridae*, of which two clades have been identified: clade I (Central Africa, Congo Basin) and II (West Africa)<sup>1</sup>. These clades exhibit variations in epidemiological and clinical features, as well as for mortality rates, supporting their classification. The virus was first isolated from captive primates in Denmark in 1958, hence its original name as “monkeypox”. First human case was reported in the Democratic Republic of the Congo in 1970, involving a 9-month-old child<sup>2</sup>. Half a century later, the World Health Organization (WHO) renamed the disease Mpox<sup>3</sup>. This virus is transmitted from infected animals to humans primarily by bites, scratches, or meat ingestion. Human-to-human transmission has been described as associated with direct contact through skin, mucous membranes, and, to a lesser extent, respiratory tract, or indirect contact through contaminated objects<sup>4</sup>. The reservoir remains unknown, but it is considered likely to be small mammals such as squirrels or rodents<sup>4,5</sup>.

On May 21<sup>st</sup>, 2022, the WHO issued an alert report on human cases of Mpox in several non-endemic countries with interhuman transmission and clinical features different from those previously described<sup>6</sup>. This led to the declaration of a Public Health Emergency of International Concern (PHEIC), reporting infections in 115 countries, with an estimated 91 123 confirmed cases and 157 deaths globally by September 30, 2023<sup>7,8</sup>. However, on May 10<sup>th</sup>, 2023, the WHO announced that this multinational outbreak no longer constitutes a PHEIC, due to the marked decrease in number of cases and deaths and the absence of significant changes in the epidemiology of the infection in previous weeks<sup>9</sup>.

Throughout the outbreak, a heightened prevalence of sexually transmitted infections (STIs) was reported, with the group of men who have sex with men (MSM) being the most affected<sup>10-12</sup>. Overall prevalence reported that between 38% and 50% of Mpox cases occurred in people living with HIV (PLWH)<sup>13</sup>. The majority of PLWH coinfecting with Mpox in different published series presented undetectable plasma viral load and good immunological status (CD4+ T lymphocytes >500 cells/mm<sup>3</sup>) with clinical characteristics and evolution similar to HIV-negative

patients<sup>14</sup>. While some reports linked HIV infection to increased hospitalization and severe Mpox symptoms, others suggested a potential correlation with detectable viral loads or low CD4+ T cell counts leading to severe disease, longer course and/or greater number of complications<sup>10,12,15,16</sup>.

In Argentina, between epidemiological weeks 21/2022 and 11/2023, 1129 Mpox cases were confirmed, resulting in two deaths, both associated with risk factors. The median age mirrored global trends at 35 years, with 98% being males from large urban conglomerates<sup>17</sup>.

According to official estimates for 2021, Argentina has a population of approximately 140 800 PLWH, who have free access to diagnosis, care, and treatment. Unlike other countries in the region, approximately 35% receive care in the private subsystem, while the largest proportion is under care in the public health subsector<sup>18</sup>. To our knowledge, there are no studies describing the characteristics of Mpox infection in PLWH in Argentina, and reports from the region are also limited.

The aim of our study was to describe the clinical and epidemiological characteristics of the Mpox outbreak in the Metropolitan Area of Buenos Aires analyzing the differences between people living with and without HIV in terms of hospitalization, complications, and mortality.

## Materials and methods

### Design

The VIHPOX study (Clinical and epidemiological characteristics of Mpox in a population with and without HIV)

is a multicenter ambispective cohort study conducted in public and private hospitals and outpatient HIV/STIs clinics, constituted as a research consortium. Its objective was to evaluate the clinical and epidemiological characteristics of PLWH coinfecting with Mpox, as well as the characteristics of this emerging disease in a population without HIV. Centers were mainly located in the city of Buenos Aires and nearby municipalities of the province of Buenos Aires, known as Metropolitan Area of Buenos Aires (MABA). Approval was obtained in each center by their respective institutional ethics committee before starting enrollment. The list of centers and number of patients recruited by site is in Table 1. The study began recruiting patients in September 2022 and ended in May 2023. If the investigator could verify the occurrence of past infection, patients could be included in the study regardless of the time elapsed since Mpox episode. Patients included before September 2022 were included retrospectively and the rest, prospectively.

### Participants

Study staff at each site offered individuals with Mpox to participate in the study, either during a face-to-face (outpatient or hospitalization) or virtual (via mobile devices; video consultation) medical consultation. Informed consent was obtained for each subject before inclusion. Regarding the inclusion criteria, population >18 years old who attended any of the participating centers and who had either ongoing or resolved Mpox infection was considered. A person was defined as living with HIV based on the history of a positive Enzyme-Linked Immunosorbent (EIA) Assay plus Western blot or baseline detectable viral load. Based on the analysis performed by the principal investigator of each center, cases of Mpox were classified as:

- Confirmed: reactive PCR (Polimerase Chain Reaction) for Monkeypox virus in clinical samples.

**Table 1** | Participant sites (and city) in VIHPOX study (clinical and epidemiological characteristics of Mpox in a population with and without HIV), period 2022-2023. Values are numbers (percentages) of patients recruited

Site	N (%)
Hospital J. Fernández (Buenos Aires)	82 (32.9)
Centro de Estudios Infectológicos (Buenos Aires)	72 (28.9)
Helios Salud (Buenos Aires)	53 (21.3)
Hospital C. Argerich (Buenos Aires)	17 (6.8)
Hospital T. Álvarez (Buenos Aires)	9 (3.6)
Hospital Municipal de Boulogne (Boulogne)	9 (3.6)
Hospital Español de la Plata (La Plata)	4 (1.6)
Hospital Houssay (Vicente López)	1 (0.4)

- Probable: clinical condition and compatible epidemiology without confirmatory microbiological studies according to the criterion of suspected case “situation 1” (characteristic rash or proctitis + contact with a confirmed case) of the Ministry of Health plus exclusion of other pathologies<sup>19</sup>.

- Neglected: those with negative PCR studies, low clinical suspicion, or alternative diagnoses.

Data were recorded anonymously in a Redcap database (Research Electronic Data Capture, Vanderbilt University, USA). A case report form was prepared based on the Mpox epidemiological form approved by the Argentinian Ministry of Health including information on sociodemographic variables, onset of signs and symptoms, comorbidities, history of smallpox vaccination, clinical manifestations, and microbiological diagnosis. Concomitant bacterial sexually transmitted infections (STIs), complications (bacterial superinfection, chronic pain, extensive non-infectious tissue necrosis, and pneumonia), hospitalization, and deaths were also recorded. Operationalization of comorbidities and complications is described in Table 2<sup>20-27</sup>. In the PLWH group, additional information regarding time of infection, antiretroviral treatment, and CD4+ T-cell lymphocyte count was registered.

### Statistical analysis

Categorical variables were described using absolute and relative frequencies and compared using the Chi-square test concerning between-group differences. We described continuous variables using medians with interquartile ranges (IQRs). Normality tests were performed for numerical variables using the Kolmogorov Smirnov or Shapiro Wilk test, as appropriate according to the number of available data. All tests were two-tailed and were considered significant if p value was less than 0.05. Missing data imputations were made in some variables and modifications were verified according to sensitivity analysis, excluding themselves from the analysis when interpretative changes were presented. Variables with multiple missing values were excluded from the analysis.

To investigate the effect of different factors on Mpox hospitalization, we performed a multivariate analysis using a multivariable logistic regression model. Variables evaluated included: HIV status, complications, rectal involvement, age, comorbidities, and concomitant bacterial STIs. Same analysis was performed in the PLWH subpopulation considering, in addition, CD4+ T lymphocyte count. SPSS version 25 software was used for these analyses.

## Results

### Epidemiological curve and demographic characteristics

The first individual consulted with onset of symptoms on June 27<sup>th</sup>, 2022, and the last one did so on February 17<sup>th</sup>, 2023, with the peak of incidence being during the week of September 25<sup>th</sup>, 2022 (epidemiological week 39). The epidemiological curve is presented in Figure 1.

A total of 258 subjects with suspected Mpox were evaluated, of whom 77% were enrolled prospectively. Median age was 36 years, with a clear predominance of male subjects (98%) who identified themselves as MSM (93.7%); 182 (73.4%) of them had a previous diagnosis of HIV infection and only fourteen of those HIV negatives were on pre-exposure prophylaxis (PrEP). The predominant form of acquisition was direct physical contact (including sexual intercourse with casual partners), group sex (32 of 137 with available data, 23.3%) and chemsex (24 of 137 with available data, 17.5%); 58.3% of participants reported social networks use for sexual encounters and 25.2% had concomitant bacterial STIs, without difference between those with and without HIV. These included syphilis at any stage (76%), urethritis without etiology (9%), gonorrhea (7%), and *Chlamydia* spp. infection (3%). Among the study participants, 210 individuals were tested for HBsAg (Hepatitis B surface antigen), with 8 (3.8%) showing reactive results. For HCV Ab (Hepatitis C virus antibody), 205 individuals were tested, and 9 (4.3%) were found to be reactive. Non-infectious comorbidities were described in 27% (n=70), being the most frequent: smoking (28.5%), substance abuse (12.8%), hypertension (10%), neuropsychiatric pathology (8.5%), alcoholism (4.2%) and obesity (2.8%). Baseline characteristics are summarized in Table 3. Median (interquartile range) time until epidemiological discharge was 21 (21-21) days. The longest time until epidemiological discharge was 48 days.

### Clinical presentation, diagnosis, and evolution

A total of 247 patients evaluated were defined as Mpox cases: 236 were confirmed and 11 were classified as probable; 23.1% of them had a previous medical appointment in another health center without concern of Mpox.

**Table 2** | Operationalization of complications and non-infectious comorbidities in VIHPOX study (2022-2023)

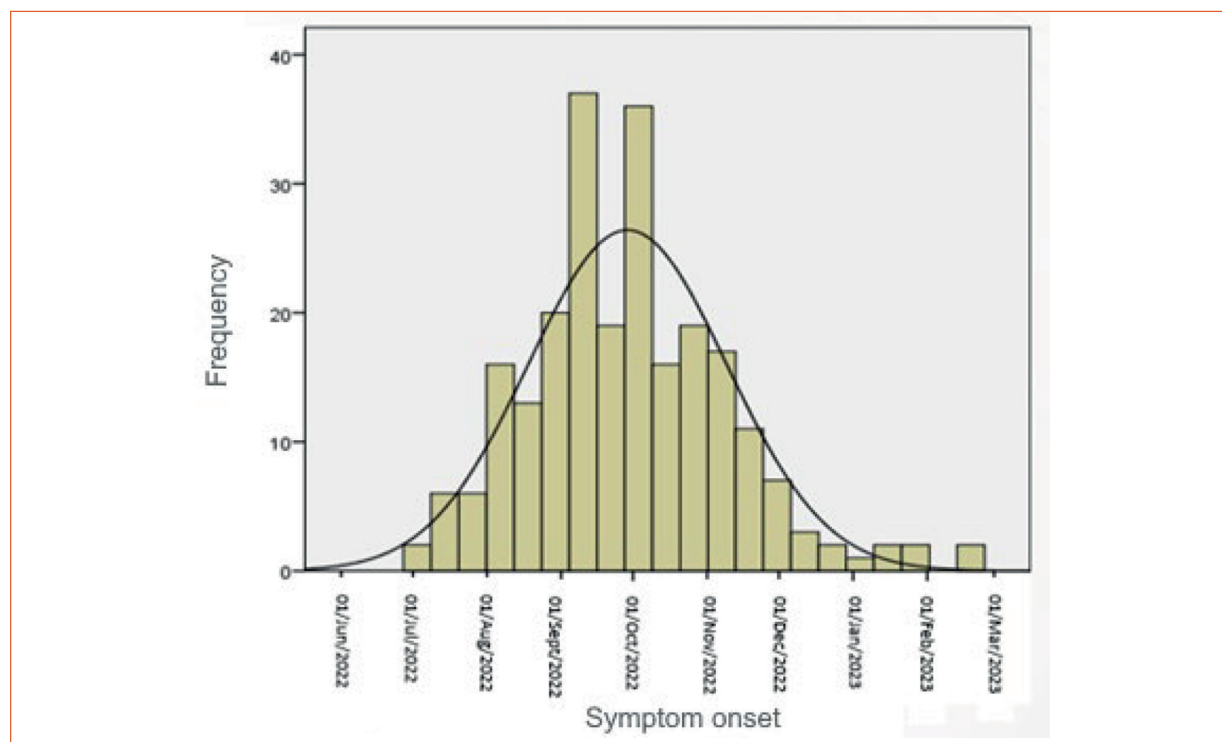
Category	Variable	Definition	Inclusion criteria	Evaluation method
Complications	Chronic pain	Persistent pain lasting after resolution of primary skin lesions	Patient reports pain after lesion resolution	Pain scale (e.g., McGill Pain Scale); record location and duration <sup>20</sup>
	Bacterial superinfection (Mild)	Infection requiring oral antibiotics, no hospitalization	Clinical signs of infection, confirmed by culture/lab tests, treated with oral antibiotics	Review of medical records, culture/lab results <sup>21</sup>
	Bacterial superinfection (Severe)	Infection requiring IV antibiotics and/or hospitalization	Clinical signs of severe infection (e.g., high fever, sepsis), requiring IV treatment/hospitalization	Review of medical records, culture/lab result <sup>21</sup>
	Non-infectious tissue Necrosis	Tissue damage or death without bacterial infection.	Evidence of tissue death caused by a skin lesion without signs of bacterial infection or trauma	Review of medical records, clinical observation <sup>21</sup>
	Pneumonia	Lung infection confirmed by chest X-ray and symptoms	Radiographic and clinical evidence of lung infection	Review of medical records, chest X-rays, lab results <sup>22</sup>
Comorbidities	Smoking	Current or historical tobacco use	≥100 cigarettes in lifetime, currently smokes or quit in last 6 months	Survey on smoking history <sup>23</sup>
	Substance abuse	Non-medical use of psychoactive substances (*)	Non-medical substance use in last 6 months	Survey on substance use history
	Hypertension	BP ≥140/90 mmHg or use of antihypertensive medications	Previous hypertension diagnosis or BP measurements meeting criteria	Review of medical records, BP measurements <sup>24</sup>
	Neuropsychiatric pathology	Previous diagnosis of mental/neurological disorders	Previous diagnosis of mental/neurological disorder	Review of medical records, mental health history survey <sup>25</sup>
	Alcoholism	Problematic alcohol use affecting health/social functioning	Excessive alcohol consumption in last 6 months or previous alcohol use disorder diagnosis	Survey on alcohol consumption history <sup>26</sup>
	Obesity	BMI ≥ 30 Kg/m <sup>2</sup>	BMI ≥ 30 Kg/m <sup>2</sup>	BMI measurement <sup>27</sup>

BP: blood pressure; BMI: body mass index; (\*) *Illegal drugs: cocaine, heroin, methamphetamine, ecstasy (MDMA), Prescription medications used without prescription or in ways other than prescribed: opioids, benzodiazepines, stimulants, Synthetic drugs: synthetic cannabinoids*

Clinical manifestations included papular (62%), pustular (60%), vesicular (48%), macular (22.9%) skin rash; scabs (45.7%); 59.4% of individuals presented with more than 20 lesions in variable evolutionary stages (Fig. 2). There was a high frequency of genital (59.6%) and rectal (25.6%) involvement.

In most cases, there were systemic manifestations such as fever (62.8%), lymphadenopathy (52%), and myalgia (39.5%). Details about predominant signs and symptoms are described in Table 4.

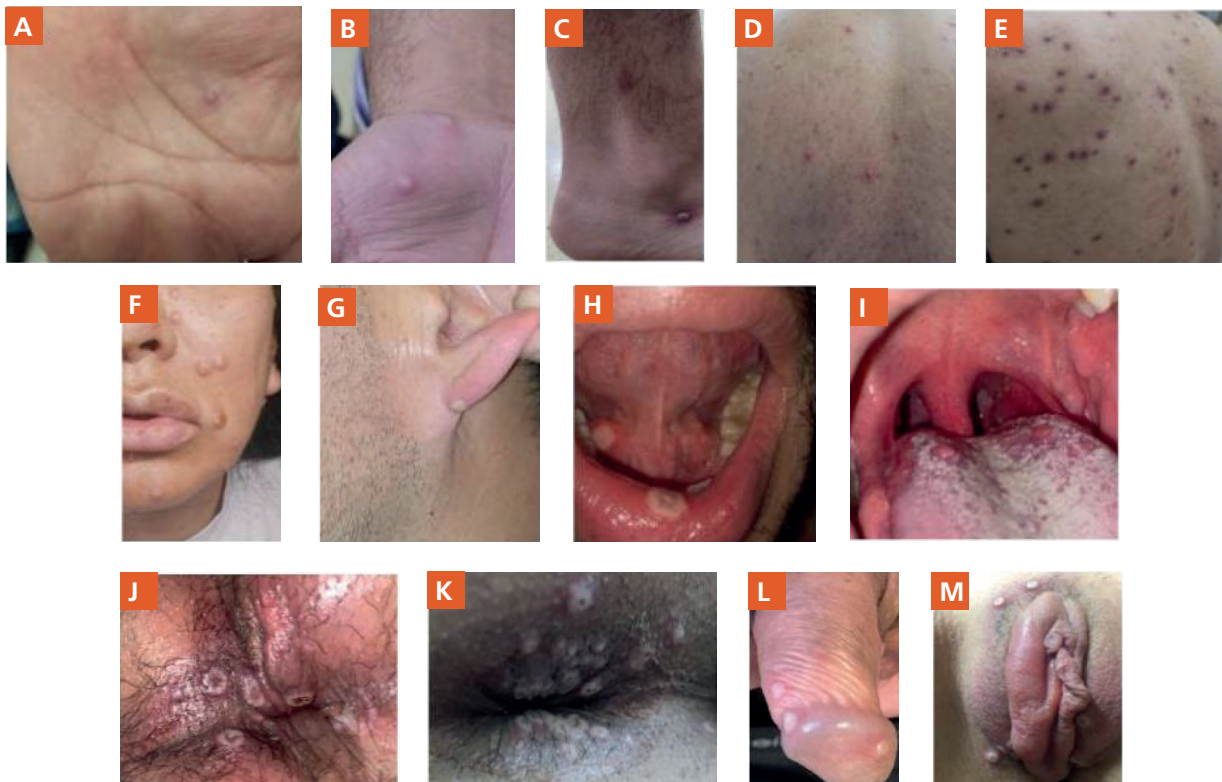
Complications occurred in 9.7% (n = 24) of cases (Fig. 3). These included: mild bacterial superin-

**Figure 1** | Epidemiological curve of Mpox cases in the Metropolitan Area of Buenos Aires**Table 3** | Characteristics of the population with Mpox in centers from the Metropolitan Area of Buenos Aires, Argentina, 2022-2023 (N = 247). Values are numbers (percentages) unless otherwise noted

	N (%)
Age (median, IQR*)	36 (30-42)
Male sex	242 (98)
Men who have sex with men (MSM)	227 (93.7)
HIV Status	
Positive	182 (73.7)
- Viral load < 50 c/mL, %	143 (79)
- CD4+ T-cell count, median (IQR*)	695 (533-948)
Negative	59 (23.8)
Unknown**	6 (2.4)
Smallpox vaccination (n=244)	
Yes	8 (3.3)
No	197 (80.7)
Unknown	39 (16)
Concomitant bacterial STIs	62 (25.1)
Recent contact with Mpox case	63 (25.6)
- Physical contact (including sexual contact)	57 (91)
- Close contact without respiratory protection	3 (4.5)
- Contact with contaminated materials	3 (4.5)
Contact with travelers	31 (12.5)
Travel in the last 21 days	25 (10.1)
Sexual intercourse in the past 21 days (n=234)	216 (92.3)
N of sexual partners in the last 6 months (median, IQR)	4 (2-10)

\*IQR= interquartile range; \*\* HIV test not taken or declined by patient or result not available

**Figure 2** | Cutaneous and mucous manifestations of Mpox in an outbreak in the Metropolitan Area of Buenos Aires: vesiculopustular lesions in extremities (A, B, C); pustular lesions with evolution to crust (D, E); facial lesions (F, G); ulcerated and vesicular lesions in oral mucosa (H, I); lesions in perianal region (J, K), penis (L) and vulva (M)



fection (n = 14), severe bacterial superinfection (n = 6), chronic pain (n = 3), extensive noninfectious tissue necrosis (n = 2), and pneumonia (n = 1).

A total of 17 patients (6.9%) required hospitalization, with a median length of 5 (2-10) days. One patient died (0.4%): a person with advanced HIV infection (CD4+ T-lymphocyte count: 14 cells/mL) who presented with extensive necrotizing lesions. Two patients (0.8%) presented sequelae: one case with a keloid-type scarring in the balanoprepucial groove and the other one with retractable scar lesions in nails. Regarding therapy, only one patient received tecovirimat (the deceased case) and 7 received corticosteroids.

#### **Characteristics of People Living with HIV with Mpox**

About 4% (n=7) of PLWH were diagnosed with HIV infection in the context of the Mpox episode. The rest had their HIV diagnosis before the Mpox episode: 25%, 1-4 years; 32%, 5-9 years;

22%, 10-14 years; 8%, 15-19 years, 13% unknown time. Of them, 92% were on antiretroviral treatment and 79% had viral load <50 copies/mL in the last 12 months. In those with detectable viremia, median viral load was 10 563 (111-37 120) copies/mL. Median CD4+ T cell count was 695 (533-948) cells/mL. Only 11 and 4 had levels under 350 and 200 cells/mL, respectively.

Compared with HIV-uninfected population, no significant differences were observed in terms of epidemiological and clinical variables except for a higher frequency of perianal lesions (19.4% vs. 38.6%,  $p = 0.009$ ) and proctitis (11.3% vs. 30.2%,  $p < 0.005$ ). There were no differences regarding complications and hospitalization. Comparison of selected variables between both populations is detailed in Table 5.

#### **Variables associated with hospitalization**

Through a multivariate analysis of the overall study population, we observed that the follow-

**Table 4** | Clinical characteristics of Mpxo in patients assisted in participant sites in the Metropolitan Area of Buenos Aires, Argentina (n = 247) during 2022-2023 outbreak. Values are numbers (percentages)

	N (%)
<b>Skin lesions*</b>	
Papules	160 (62)
Pustules	155 (60)
Vesicles	124 (48)
Scabs	118 (45.7)
Macules	59 (22.8)
<b>Localization†</b>	
Genital	154 (59.6)
Upper limbs	121 (46.8)
Trunk	119 (46.1)
Face	106 (41.8)
Perianal region	87 (33.7)
Lower limbs	81 (31.3)
Oral cavity	46 (17.8)
Conjunctival lesions	2 (0.7)
Other	7 (2.7)
<b>Systemic signs and symptoms</b>	
Fever	162 (62.8)
Lymphadenopathy	134 (51.9)
Myalgia	102 (39.5)
Weakness	101 (39.1)
Headache	99 (38.4)
Sore throat	50 (19.4)
Back pain	35 (13.6)
Penile edema	21 (8.1)
Proctitis	66 (25.6)
Anal pain	59 (22.9)
Tenesmus	24 (9.39)
Bleeding	17 (6.6)

\* Lesions at different stages could coexist in the same patient

† Lesions could occur in different anatomical sites simultaneously

ing variables were associated with hospitalization: presence of non-infectious comorbidities (Odds Ratio: 3.47, 95% CI: 1.22-9.86;  $p < 0.01$ ) and complications (Odds Ratio: 17.91, 95% CI: 5.85-54.79;  $p < 0.01$ ). HIV status did not increase the chance of hospitalization.

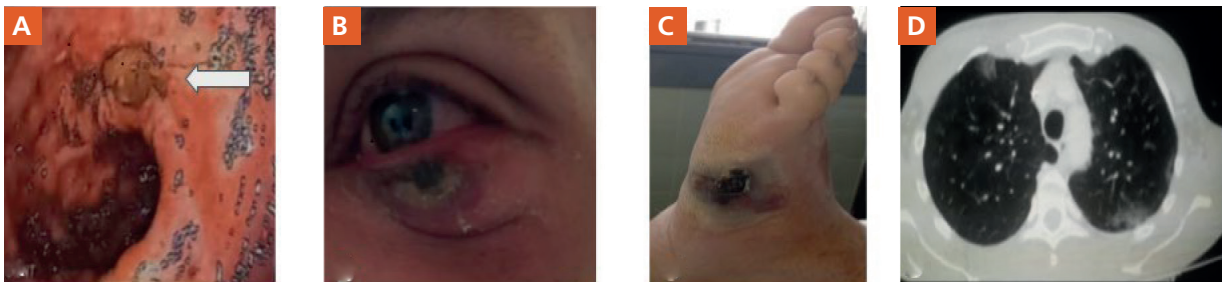
In PLWH, only the presence of complications was associated with hospitalization, as detailed in Table 6. When this population was analyzed according to CD4+ T-cell count, those with less than 350 cells/mL were more likely to have complications but not hospitalization, as detailed in Table 7.

## Discussion

In our study, Mpxo infection occurred in a young population, mostly MSM with a history of recent sexual exposure. We describe the clinical manifestations and factors associated with hospitalization in people with and without HIV. The epidemiological characteristics of our population were similar to other publications. In a CDC report between May and December 2022, of a total of 29 980 confirmed and probable cases aged between 15 to 64 years, MSM predominated, with an incidence in urban areas (where 85% of the population resides) in this age group of



**Figure 3** | Proctitis due to Mpox (A): ulcerated irregular mucosa (arrow) with fibrin deposits. Cutaneous complications: periorbital cellulitis from ulcerated Mpox lesion (B), non-infectious necrotizing lesion in foot (C). Pulmonary involvement with ground-glass lesions (D)



**Table 5** | Comparison of selected epidemiological and clinical characteristics of Mpox in population with and without HIV in the metropolitan area of Buenos Aires, Argentina (2022-2023)

	People without HIV (n = 59)	People with HIV (n = 182)	p
Age (median, IQR*)	31 (27-38)	38 (32-43)	NS
Male sex at birth, n (%)	54 (91.5)	182 (100)	NS
Recent contact with Mpox case, n (%)	17 (29)	46 (25.4)	NS
Sexual intercourse in the last 21 days, n (%)	50 (83.9)	153 (84.1)	NS
N of sexual partners in the last 6 months, median (IQR*)	5 (3-10)	4 (2-10)	NS
Group sex, n (%)	12 (21)	18 (10)	NS
Perianal lesions, n (%)	11 (19.4)	70 (38.6)	0.009
Proctitis, n (%)	7 (11.3)	55 (30.2)	<0.005
Hospitalization, n (%)	6 (9.7)	11 (5.8)	NS
Complications, n (%)	8 (12.9)	15 (8.5)	NS

\*IQR= interquartile range; NS: non-significant

**Table 6** | Factors associated with hospitalization during the Mpox epidemic in people living with HIV (2022-2023) in the Metropolitan Area of Buenos Aires, Argentina (n = 182)

	OR*	Lower limit	Upper limit	p
Comorbidities	1.55	0.39	6.17	0.52
Complications	17.89	4.71	67.95	<0.01
CD4+ <500 cells/mm <sup>3</sup>	0.68	0.10	2.31	0.35*
Proctitis	0.48	0.10	2.31	0.35

\*For CD4+ values <350 cells/mL, p >0.05

**Table 7** | Multivariate analysis considering clinically relevant conditions and events in people living with HIV with CD4+ T-lymphocyte count <350 cells/mm<sup>3</sup> coinfecting with Mpox in the Metropolitan Area of Buenos Aires, Argentina (2022-2023)

	OR*	Lower limit	Upper limit	p
Comorbidities	1.97	0.81	4.76	0.12
Complications	3.25	1.08	9.72	0.02
Hospitalization	2.12	0.51	8.71	0.28
Proctitis	0.92	0.39	2.14	0.85

\*OR: Odds ratio

13.5 per 100 000<sup>28</sup>. In the data provided by GeoSentinel network, with information collected from 18 sites in 15 countries between May and July 2022 from 226 patients, median age was 37 years, all of them male, 98% MSM, 8% had had a trip abroad within the previous 3 weeks and the median of sexual partners was 3. In this report, 44% were PLWH, with a median CD4+ T lymphocytes of 713 cells/mL; only one patient had CD4+ T cell count <200 cells/mL. Although prevalence of HIV infection in this study was lower than in our report, both populations had an overall good immune status<sup>29</sup>. Considering data from Latin America, in an observational cohort study conducted between June and August 2022 in Rio de Janeiro, Brazil, the authors described that, of 342 individuals with suspected Mpox, 60.8% were confirmed cases representing 49.3% of the total reported in that district<sup>14</sup>. It is noteworthy that the prevalence of confirmed cases in our cohort was considerably higher, which can be attributed to methodological differences between both studies. Like in our report, patients were mostly young and MSM. Of them, 95% reported sexual contact in the previous month, and 22.4% sexual contact with a probable case of Mpox. One third of confirmed Mpox cases were receiving pre-exposure prophylaxis (PrEP), a significantly higher percentage than in our report. This is attributed to the fact that Brazil has a well-developed PrEP strategy with logistics in place, unlike Argentina which is in the early stages of its implementation. History of vaccination against smallpox was also infrequent in this cohort (8.2%) but higher than in our study (3.3%).

Prevalence of other STIs in the context of Mpox was considerable high. One quarter of the population presented concomitantly with another STI: 25.4% in PLWH and 27.4% in the HIV-negative population, as shown in reports from other countries. In London, Girometti et al. reported that the percentage of STIs concomitant with Mpox in PLWH attending a sexual health clinic was 31%<sup>30</sup>. In a case-control study, the authors found that those with a confirmed Mpox diagnosis were more likely to have had an STI in the previous year or to have it concurrently<sup>31</sup>. Despite these findings, researchers at Duke University Health System reported that most patients evaluated for Mpox were not studied for

other STIs. However, its prevalence was high when these studies were conducted<sup>31,32</sup>. From the GeoSentinel report, 15% of patients had concomitant STIs: 5% gonorrhea, 3% primary or secondary syphilis, and 2% *H. simplex*, among the most frequent ones<sup>29</sup>. Considering regional data, in the Rio de Janeiro cohort, accompanying STIs were found in 33% of patients: gonorrhea (9.9%), *Chlamydia* spp. (10.6%), and active syphilis (21.2%)<sup>14</sup>. The high prevalence of concomitant STIs reported by other authors, as well as in this study, supports the need to develop diagnostic techniques that allow simultaneous diagnosis of multiple infections to strengthen other STIs screening when there is a clinical suspicion of Mpox<sup>33</sup>.

Regarding clinical presentation, skin lesions were practically universal in our cohort and most of our patients presented fever and lymphadenopathy as predominant systemic signs. This finding does not differ from the Brazilian cohort where 83.2% of individuals presented general symptoms, 76.1% disseminated skin rash, 77.3% genital, 33.1% anal, and 37.1% rectal lesions<sup>14</sup>. In the Geosentinel report, 99% had a rash most frequently in the genital area, followed by perianal area, trunk, and extremities; 58% had lesions in the same evolutionary stage and the rest of them with variable evolutionary stages, as occurred in our series<sup>29</sup>. Likewise, the rate of complications and hospitalization did not differ from previous communications<sup>14,29</sup>. In our cohort, 9.7% had complications, 6.9% required hospitalization, and one patient with advanced HIV died due to a necrotizing form of Mpox. This is coincident to what was described in the Rio de Janeiro cohort where 9.1% required hospitalization, being the most frequent reasons: pain management, bacterial superinfection, and paraphimosis. Only one patient required intensive care and mechanical ventilation, and there were no deaths<sup>14</sup>. In the GeoSentinel report, 13% of patients required hospitalization and none required intensive care. Most frequent causes of hospital admission were severe illness, pain management, and isolation requirement. No deaths were reported<sup>29</sup>. A Colombian report of 521 cases also described two deaths corresponding to PLWH: one of them with advanced disease and another one with a recent diagnosis without immuno-

logical or virological studies<sup>34</sup>. Evaluating the characteristics of Mpox in PLWH was one of the priorities in the context of the epidemic. Our series describes a higher frequency of proctitis or perianal lesions in this population. It is of clinical importance for the management of Mpox in this group to investigate anorectal involvement during clinical examination. On the other hand, our series does not describe HIV status itself as a variable associated with a higher frequency of complications or hospitalization, which is consistent with other reports<sup>14,29</sup>. This could be attributed to the fact that most of our patients were on antiretroviral treatment, with undetectable viral load and good immunological status. Also, the number of individuals with advanced HIV disease was low. However, in a retrospective review of the literature describing 27 cases of Mpox/HIV coinfection, two cases were fatal, both with CD4+ T lymphocytes <100 cells/mL<sup>35</sup>. An international multicenter study evaluated the clinical features and complications of Mpox in PLWH with a CD4+ T cell count <350 cells/mL or CDC stage C. Among 382 patients, the majority were men, with a median age of 35 years. Median CD4+ T-cell count was 211/mL; 22% with <100 cells/mL and 25% between 100-200 cells/mL. Serious complications were more common in patients with CD4+ <100 cells/mL compared to those with more than 300 cells/mL, including necrotizing skin lesions, lung involvement, secondary infections, and sepsis. The overall hospitalization rate was 28%, of which a quarter died. All deaths occurred in patients with CD4+ <200 cells/mL<sup>36</sup>. The authors concluded that Mpox may occur in patients with advanced HIV disease with necrotizing forms, as happened with the only deceased patient in our cohort. This would allow the hypothesis that these forms of Mpox could constitute a defining condition of AIDS due to the higher prevalence of fulminant disease, systemic manifestations, and death. Although our study is limited by the low number of patients with CD4+ counts <350 cells/mL, the higher frequency of complications described in this group would support this hypothesis.

Regarding HIV diagnosis, 3.7% of PLWH in our study were diagnosed in the context of the Mpox episode. This supports the importance and benefits of increasing HIV testing in the context of

outbreaks. The Mpox outbreak made it possible to make new HIV diagnoses and even, based on experiences from other countries, to link patients with the healthcare system<sup>37,38</sup>. Those individuals in whom HIV infection have been ruled out but remain at risk, should be linked to prevention services for counseling, PrEP and other combined prevention tools.

The epidemiology of the international Mpox outbreak was unusual since cases described in outbreaks from non-endemic areas were not related to travel to endemic areas and transmission was predominantly sexual in MSM. In high-resource countries, vaccines available to deal with the recent outbreak were ACAM2000 and MVA-BN. ACAM2000 is a second-generation live attenuated vaccine against the vaccinia virus approved for the Food and Drug Administration (FDA) for use before or after exposure to Mpox<sup>39</sup>. Argentina did not have access to active immunization as no vaccine was available in the country. Despite this, the outbreak was self-limited, without new cases reported in any of the participating centers from February 2023 until the end of our study in May. This pattern is similar to that observed in other countries with access to vaccination<sup>40</sup>. However, it raises the question of how many people with risky behaviors for Mpox remain susceptible and might generate new outbreaks in the future. The Democratic Republic of Congo (DRC) has experienced a significant Mpox outbreak in 2024, with over 16 000 reported cases across all provinces, including more than 2600 confirmed cases and 511 fatalities. This represents a 3% case fatality rate and marks the largest outbreak of Clade I Mpox in Africa. The epidemic has spread beyond DRC's borders, with confirmed cases reported in five neighboring countries: Burundi, Central African Republic, Congo, Rwanda, and Uganda. Additionally, Kenya documented its first Mpox case in late July 2024. Genetic analysis has revealed the presence of Mpox clade Ia in cases from the Central African Republic and Congo. A new variant, Mpox clade Ib, was first identified in DRC in April 2024 and has since been detected in Burundi, Rwanda, Uganda, and Kenya. In response to the escalating situation, the Africa Centers for Disease Control officially classified Mpox as a Public Health Emergency of Continental Secu-

riety on August 13, 2024. The following day, the World Health Organization elevated the outbreak to the status of a public health emergency of international concern<sup>41</sup>. On 16 August 2024, Argentinian Ministry of Health issued a national report due to the emergency of a new Mpxo variant associated with sustained transmission as well as cases on a wider age range including children<sup>42</sup>.

Our study has several limitations. It had an observational design, which encompassed a limited geographical area, but it should be noted that the MABA was considered the epicenter of the epidemic in our country. PLWH had a good immunovirological profile, with very few individuals with advanced disease to evaluate an association with hospitalization or mortality. Conversely, we could observe more complications in this group. In addition, given the lack of access to vaccination, we couldn't assess its potential impact on the clinical presentation. Despite its limitations, our study extends current knowledge about Mpxo to the regional level, covering a significant

percentage of the country's total cases (1140 cases reported as of October 1, 2023) and comparing people living with and without HIV<sup>43</sup>. It also describes comorbidities, along with complications, as factors associated with hospitalization. Consequently, presence of comorbidities (other than HIV infection) should be considered when clinically evaluating the patient, requiring close monitoring. On the other hand, in PLWH only the presence of complications was associated with hospitalization. When analyzing the subgroup of patients with CD4+ <350 cells/mL, an association was found with a higher frequency of complications, but not with hospitalization.

Finally, although the number of Mpxo cases has decreased in our country, we must consider this emerging disease as another sentinel event that highlights the need to build and maintain the clinical infrastructure that strengthens the prevention and response to epidemics involving STIs<sup>44</sup>.

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