

Elsevier has created a <u>Monkeypox Information Center</u> in response to the declared public health emergency of international concern, with free information in English on the monkeypox virus. The Monkeypox Information Center is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its monkeypox related research that is available on the Monkeypox Information Center - including this research content - immediately available in publicly funded repositories, with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the Monkeypox Information Center remains active.

oa

Epidemiological and clinical characteristics of patients with human monkeypox infection in Mexico: A nationwide observational study

Isaac Núñez,^{a,i} Miguel García-Grimshaw,^{b,i} Santa E. Ceballos-Liceaga,^{c,i} Carla Toledo-Salinas,^d Guillermo Carbajal-Sandoval,^c Luisa Sosa-Laso,^c Gabriel García-Rodríguez,^c Ricardo Cortés-Alcalá,^e Alethse de la Torre,^f Sergio Fragoso-Saavedra,^a Alejandro Quintero-Villegas,^a Hugo López-Gatell,^{e,**,j} Gustavo Reves-Terán,^{d,***,j} and Sergio Iván Valdés-Ferrer^{b.g,h,*,j}

^aDepartment of Medical Education, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, 14080, Mexico ^bDepartment of Neurology and Psychiatry, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, 14080, Mexico

^cDirección General de Epidemiología, Secretaría de Salud, Gobierno de México, México City, 01480, Mexico ^dComisión Coordinadora de Institutos Nacionales de Salud y Hospitales de Alta Especialidad, Mexico City, 14610, Mexico

^eSubsecretaría de Prevención y Promoción de la Salud, Secretaría de Salud, Gobierno de México, México City, 06600, Mexico

^fCentro Nacional para la Prevención y el Control del VIH y el SIDA, Mexico City, CP 06140, Mexico

⁹Department of Infectious Diseases, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, 14080, Mexico ^hInstitute of Bioelectronic Medicine, Feinstein Institutes for Medical Research, Manhasset, NY, 11030, USA

Summary

Background Human monkeypox, a zoonosis historically endemic to West and South Africa, has led to a worldwide outbreak driven by human-to-human transmission resulting in an international public health emergency. Endemic and outbreak monkeypox cases may differ in their affected populations, clinical features, and outcomes. Thus, profiling cases of the current monkeypox outbreak worldwide is crucial.

Methods We performed a nationwide observational surveillance-based study from May 24 to September 5, 2022. Patients that met the operational clinical definition of monkeypox or symptomatic close contacts of confirmed cases were tested by real-time polymerase chain reaction. Clinical data were collected with a standardized case-report form. We report epidemiologic, sociodemographic, and clinical characteristics of confirmed cases.

Findings Five-hundred and sixty-five human monkeypox confirmed cases were analysed; 97.2% were men, of whom 59.5% identified as men who have sex with men, and 54.5% had human immunodeficiency virus infection. The median age was 34 years. All patients but one had rash (99.8%), 78.9% had fever, and 47.8% reported myalgia. The anogenital area was the most commonly affected one by rash (49.6%), and proctitis occurred in 6.2% of patients. Six patients required hospitalization, of which one died due to causes unrelated to monkeypox.

Interpretation The 2022 monkeypox outbreak in Mexico is mainly driven by middle-aged men who have sex with men, of which a large proportion are persons who live with human immunodeficiency virus infection. Clinical features such as the high proportion of anogenital lesions suggest sexual contact is a pivotal transmission mechanism in this outbreak.

Funding This research was supported by grant A1-S-18342 from Consejo Nacional de Ciencia y Tecnología (CONACyT), Mexico (to S.I.V.-F.).

Copyright © 2022 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Keywords: Monkeypox virus; Orthopoxvirus; Mexico; Epidemiology; Viral zoonosis

1

^{*}Corresponding author. Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Vaso de Quiroga 15, Tlalpan, CDMX, 14080, Mexico. **Corresponding author. Subsecretaría de Prevención y Promoción de la Salud, Secretaría de Salud, Gobierno de México, México City, 06600, Mexico. ***Corresponding author. Comisión Coordinadora de Institutos Nacionales de Salud y Hospitales de Alta Especialidad, Mexico City, 14610, Mexico.

E-mail addresses: hugo.lopez-gatell@salud.gob.mx (H. López-Gatell), gustavo.reyesteran@salud.gob.mx (G. Reyes-Terán), sergio.valdesf@incmnsz. mx (S.I. Valdés-Ferrer).

mx (S.I. Valdes-Ferrer).

ⁱEqual contributors and joint first authors.

^jEqual contributors and joint corresponding authors.

Research in context

Evidence before this study

Monkeypox, a zoonotic infection endemic to parts of Central and West Africa, has recently caused a worldwide outbreak. We performed a PubMed search for large observational studies (>50 patients) of monkeypox cases during the current outbreak in which clinical features were described. We used the term "monkeypox" with no language restrictions and limited our search from May 1, 2022 (the date of the first reported case) until September 3, 2022. Eight studies met our criteria for inclusion. Seven of these studies were from Europe and one from the United States. Only two of the studies evaluated country-wide cases through epidemiologic surveillance. All studies reported a vast majority of affected men, with a high proportion being men who have sex with men (MSM) and an important percentage being persons living with human immunodeficiency virus (PLHIV). Rash was almost universally present, with the anogenital region being the most commonly affected area.

Added value of this study

Our country-wide study evaluated over 500 confirmed monkeypox cases in Mexico and is the first major epidemiologic study of monkeypox in Latin America. We thoroughly described sociodemographic and clinical characteristics. Akin to other studies, we also found a high percentage of men (97.2%), of which 59.5% self-identified as MSM and more than half as PLHIV. Of note, before this outbreak, data on PLHIV had been scant, and the high proportion observed in our study helps to illustrate how these patients are affected. Rash was almost universal, and we also observed that the anogenital region was the most affected area. In conjunction with the debut of proctitis as a symptom in reports of this outbreak, the aforementioned highlights that sexual contact is perhaps the pivotal mechanism of transmission during this outbreak. Additionally, we describe two paediatric and two adolescent cases, which have been so far infrequently reported. One patient died due to causes deemed unrelated to monkeypox, highlighting the potential for deaths *with* monkeypox and not *due* to monkeypox.

Implications of all available evidence

The 2022 monkeypox outbreak is occurring primarily among middle-aged MSM, many of whom are PLHIV. Close physical -particularly sexual-contact appears to be particularly relevant as a transmission mechanism. Our findings are broadly consistent with those reported elsewhere in the current outbreak and support implementing preventive measures, such as vaccination and educational efforts, aimed toward the primarily affected populations (MSM and PLHIV), with particular care to prevent stigma.

Introduction

Human monkeypox is a disease caused by a zoonotic DNA virus of the Orthopoxvirus genus.1 The monkeypox virus was discovered in primates in 1958, and the first human disease case was detected in 1970 in the Democratic Republic of Congo.2.3 Ever since, sporadic zoonotic outbreaks have been documented, mainly in endemic regions of parts of Central and West Africa.4-7 From 2017 to 2019, travel-associated monkeypox cases were reported in several countries, including a large outbreak in Nigeria.7-10 Since then, in May 2022, a confirmed monkeypox case was documented in the United Kingdom.^{11,12} By October 10, more than 71,000 cases had been reported worldwide.11 The Nigeria and current outbreaks are driven by clade II (west African clade), the less pathogenic one.1,7,11 Nonetheless, the World Health Organization (WHO) recognised this outbreak as a public health emergency of international concern on July 21, 2022.11

Given that in the past monkeypox transmission mainly occurred in low-income countries and by zoonotic transmission, little was known about the relative importance of inoculation routes during human-tohuman transmission.^{1,13} Epidemiological studies of the 2017 outbreak in Nigeria began to shed light on the potential importance of human-to-human transmission, particularly via sexual contact.^{7,14,15} Furthermore, studies of the current outbreak have found clinical pictures and transmission patterns not entirely compatible with those classically described, but similar to those of the 2017 outbreak in Nigeria.^{12,16,17} Hence, it is vital to study this disease in multiple contexts, as severity could vary between populations, including those immunocompromised and people who live with HIV (PLHIV) for whom there is limited data. Here we describe epidemiologic and clinical characteristics of laboratory-confirmed monkeypox cases in Mexico between May and September 2022.

Methods

Study design and participants

We performed a nationwide observational study based on passive epidemiological surveillance data. Deidentified clinical metadata were obtained directly from the Mexican Ministry of Health. Starting on May 24, 2022, reporting suspected monkeypox cases became mandatory in Mexico. Cases are notified to local epidemiologic authorities by the attending physicians, who turn the collected samples to the federal authorities and fill out a paper-based epidemiologic case report form (CRF, Appendix pp 2–3) adapted from other CRFs for infectious diseases with a mandatory report by law (e.g. rabies and tuberculosis). CRFs are filled by the attending clinician and record the date on which rash, fever, and other general symptoms started. Symptoms and signs are documented by combining patient self-report and physical examination by the attending clinician, including specific regions in which rash and lymphadenopathy were present. All details on possible exposures to confirmed cases were self-reported.

Operational definitions of cases were developed to determine which patient samples should be collected. Probable cases were defined as any person with one or more skin lesions (of any kind) and at least one of the following symptoms: fever, myalgia, headache, lymphadenopathy, fatigue, arthralgia, back pain, and no other condition that explained the symptoms.13 Samples were collected from probable cases in a standardized manner according to the guidelines for the management of monkeypox recently published by the Mexican Ministry of Health.13 Briefly, if the patient had vesicles or pustules, a sample of the liquid was taken. If the patient mainly had scabs, several were sampled. However, if more than one type of lesion was present, all viable ones were sampled. Finally, patients with no identifiable lesions that presented with a flu-like disease and were in contact with a confirmed case during the previous 21 days were tested with a nasal or oropharyngeal swab.

All samples were then refrigerated at 4–8°C or frozen (according to the capabilities of each referring centre) within an hour of collection and stored for up to 5 days, then sent to the National Institute for Diagnosis and Epidemiologic Reference (INDRE, for its initials in Spanish), which is the only laboratory with the capability and due processes to handle monkeypox virus samples at the time. All samples were then analysed by real-time polymerase chain reaction (RT-PCR) for monkeypox. Patients with a positive RT-PCR for monkeypox were considered confirmed cases.

Statistical analysis

We used medians, interquartile ranges, and total ranges to describe numeric data, while counts and proportions were used to describe categorical data. All analyses were performed with R version 4.1.2.

Ethics

This study was approved by the Ethics and Human Research committees of the Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán (ID: NER-4287). Due to the observational nature of the study and the use of a de-identified data set, informed consent was waived.

Role of the funding source

The funding source had no role in the design, conduction, or reporting of the study.

Results

Between May 24 and September 5, 2022, 1146 persons sought medical attention for symptoms and signs suggestive of human monkeypox infection in Mexico and were reported to the Mexican Ministry of Health. A total of 565 cases were confirmed in 26 out of 32 states (Fig. 1, Appendix Table 1). The epidemiologic curve of patients is shown in Fig. 2. All samples were identified as clade II (West African clade). The demographics and clinical characteristics of the cohort are shown in Table 1. Altogether, 97.2% were male with a median age of 34 years. Two-hundred and thirty patients (40.7%) declined to identify or did not have available data on sexual orientation/preference; however, among those who did, 97.6% were men who have sex with men (MSM), self-identifying as gay or bisexual.

Overall, 299 (52.9%) were PLHIV. HIV viral load was available for only 74 of those, of whom 66 (89.1%) had adequate viral control, as evidenced by an undetectable (\leq 50 copies/mm³) circulating HIV viral load. Fourhundred and sixty-one patients (81.6%) were unable to or declined to identify the potential source of exposure. Eight patients were healthcare workers. Only one patient died. He sought medical attention due to suspected monkeypox but was hospitalized due to clinical deterioration associated with sepsis, testing positive for HIV (circulating CD4⁺ T cell count, 7 cells/mm³), hepatitis C, and syphilis during hospitalization. He developed septic shock and respiratory failure that led to death; no other etiological microorganisms were detected in numerous cultures and serological testing performed.

Clinical findings are summarized in Tables 2 and 3. Skin lesions (rash) were an almost universal finding. However, rash by itself was the initial manifestation in only 1% of the cohort. Other common findings were fever (78.9%), myalgia (47.8%), headache (39.9%), articular pain (42.7%), lymphadenopathy (41.1%), fatigue (33.8%), and odynophagia (24.8%).

Symptoms were generally similar regardless of HIV infection status (Fig. 3 and Table 2). The distributions of the number of symptoms and number of rash regions are shown in Fig. 3A and B. Most patients only had one region involved with lymphadenopathy (Fig. 3C). In addition, the presence and location of lymphadenopathy were similar regardless of HIV infection status; however, the presence of anogenital rash was more common in PLHIV (Table 3). The most common skin lesions were papules (58.7%), and ulcers were the least common ones (10.2%). Although clinical findings were similar between females and males, not a single female patient reported proctitis (Appendix Table 2), and rash

Articles



Fig. 1: Patient selection flowchart. DGE: General Directorate of Epidemiology; HSV: herpes simplex virus; VZV: varicella-zoster virus.



Fig. 2: Epidemiologic curve of confirmed monkeypox cases in Mexico.

in the anogenital area was less frequent than in males (Appendix Table 3).

Two cases occurred in children aged 3 and 9 years old, and two additional cases were detected in adolescents aged 15 and 17. In none was sexual contact declared as the possible mode of transmission; however, the two adolescents developed proctitis. Rash and fever were the chief complaints (Appendix Tables 4–6).

Discussion

The current monkeypox outbreak is one of three diseases currently considered by the WHO to be public health emergencies of international concern (the others being polio and COVID-19).¹⁸ Monkeypox is an understudied disease despite being described over 50 years ago and outbreaks in endemic areas -warning signs to the current outbreak-have been mostly ignored.^{19–21} Given the relatively scarce literature and the classically-described zoonotic nature of the disease, much is unknown about human-to-human transmission. This knowledge gap started to be explored thanks to efforts during the Nigeria outbreak; however, much remains to be known.^{7,14} The WHO region of the Americas currently has the highest number of reported cases: over 45,000.¹¹ Brazil, Perú, Colombia, and Mexico are the Latin American countries with the most confirmed cases. Jointly they account for over 15,000 cases (about 21% of the global total).¹¹ Thus, Latin

ARTICLE IN PRESS

	Male sex (%)	Female sex (%)	All patients (%)
Number	549 (97.2)	16 (2.8)	565 (100)
Age	34 (30-41)	36 (29–42)	34 (30-41)
Recent national flight	60 (10.9)	3 (18.8)	63 (11.2)
Recent international flight	46 (8.4)	0 (0)	46 (8.1)
No recent flights	447 (81.4)	13 (81.2)	460 (81.4)
Sexual orientation ^a	-	-	-
Homosexual	316 (57.6)	0 (0)	316 (55.9)
Bisexual	11 (2)	0 (0)	11 (1.9)
Heterosexual	4 (0.7)	4 (25)	8 (1.4)
Not specified	218 (39.7)	12 (75)	230 (40.7)
Healthcare worker	10 (1.8)	0 (0)	10 (1.8)
Pregnant	0 (0)	2 (12.5)	2 (0.4)
Cared for at a public institution	500 (91.1)	15 (93.8)	515 (91.2)
Current diagnosis of			
HIV	299 (54.5)	0 (0)	299 (52.9)
Syphilis	26 (4.7)	1 (6.2)	27 (4.8)
Gonorrhea	2 (0.4)	0 (0)	2 (0.4)
Chronic hepatitis B	1 (0.2)	0 (0)	1 (0.2)
Chronic hepatitis C	10 (1.8)	0 (0)	10 (1.8)
Unspecified chronic hepatitis	4 (0.7)	0 (0)	4 (0.7)
CD4+ cell count in PLHIV (cells/mm ³) ^b	492 (328-700)	-	492 (328–700)
Undetectable viral load in PLHIV (<200 copies/mm ³) ^c	66 (89.1)	-	66 (89.1)
Possible transmission route:			
Sexual contact	94 (17.1)	0 (0)	94 (16.6)
Non-sexual contact	9 (1.6)	1 (6.2)	10 (1.8)
Unknown	446 (81.2)	15 (93.8)	461 (81.6)
Participated in group sex event	3 (0.5)	0 (0)	3 (0.5)
Number of self-reported contacts	1 (0-3)	3 (1-3)	1 (0.5-3)
Required hospitalization	5 (0.9)	1 (6.2)	6 (1.1)

Percentages may not add to exactly 100% due to rounding. Abbreviations: HIV: human immunodeficiency virus infection; PLHIV: persons living with HIV. ^aAvailable for 174 patients (171 male, 3 female). ^bAvailable for 222 patients. ^cAvailable for 74 patients, the percentage was calculated taking this number. Age and CD4 cell count are shown in median and interquartile ranges. Flights were considered recent if they occurred during the 3 weeks before symptoms started. Self-reported contacts were not necessarily sexual contacts.

Table 1: Epidemiologic and sociodemographic characteristics of patients with confirmed monkeypox.

America is a region that previously did not have human monkeypox and is now heavily afflicted by the outbreak. As such, reports detailing the characteristics of patients with monkeypox in the region are lacking. In this study, we report the clinical and epidemiological characteristics of 565 monkeypox cases in Mexico focused on three parts: characteristics of patients with monkeypox, their clinical picture, and potential transmission mechanisms.

The first large description of endemic monkeypox included roughly 50% women, and more than 90% of patients were younger than 15 years of age.⁴ In sharp contrast, the current outbreak is driven by adult males, which account for more than 99% of confirmed cases worldwide.¹¹ Recent reports describe almost uniformly a male predominance, particularly MSM, accounting for nearly 100% of patients in these cohorts.^{12,16,22,23} In our study, we also found a male predominance, accounting for more than 96% of cases. While over 57% also identified as MSM, around 40% did not have data or did not disclose a sexual preference. Thus, it is likely that the real proportion is higher. This contrasts with the Nigeria outbreak, in which a small study documenting sexual history found that most patients identified as heterosexual but is consistent with the high proportion of MSM reported in the current outbreak.^{12,16,22,24,25}

In our cohort, the median age (34 years) is consistent with that reported elsewhere.^{12,16,22,23,25} PLHIV also represent a high proportion of reported cases ranging from 21 to 41% in the aforementioned studies.^{12,16,22,23} We found a slightly higher proportion of PLHIV among our cases (~53%), but many patients did not have data on HIV status, suggesting that the actual proportion of PLHIV is underestimated. However, our results support what has been reported until now: the current monkeypox outbreak occurs primarily among middle-aged MSM, many of whom are PLHIV.^{18,26} MSM and PLHIV are unfortunately stigmatized groups, and

Articles

	Prior HIV diagnosis (%)	No prior HIV diagnosis (%)	All patients (%)		
Number of patients	299 (52.9)	266 (47.1)	565 (100)		
Incubation period ^a	8 (3-9)	7 (5-10)	8 (4-9)		
Initial symptom	-	-	-		
Rash	4 (1.3)	2 (0.7)	6 (1)		
Fever	16 (5.3)	18 (6.7)	34 (6)		
Other symptoms	107 (35.7)	95 (35.7)	202 (36)		
Concomitant rash and systemic symptoms	172 (57.5)	151 (56.7)	323 (57)		
Rash	299 (100)	265 (99.6)	564 (99.8)		
Fever	241 (80.6)	205 (77.1)	446 (78.9)		
Shivers	35 (11.7)	29 (10.9)	64 (11.3)		
Lymphadenopathies	130 (43.5)	102 (38.3)	232 (41.1)		
Fatigue	106 (35.5)	85 (32)	191 (33.8)		
Headache	136 (45.5)	112 (42.1)	248 (43.9)		
Nausea	5 (1.7)	5 (1.9)	10 (1.8)		
Vomit	2 (0.7)	4 (1.5)	6 (1.1)		
Myalgias	151 (50.5)	119 (44.7)	270 (47.8)		
Articular pain	134 (44.8)	107 (40.2)	241 (42.7)		
Lower back pain	35 (11.7)	36 (13.5)	71 (12.6)		
Proctitis	26 (8.7)	9 (3.4)	35 (6.2)		
Conjunctivitis	0 (0)	5 (1.9)	5 (0.9)		
Photophobia	1 (0.3)	0 (0)	1 (0.2)		
Cough	12 (4)	28 (10.5)	40 (7.1)		
Odynophagia	66 (22.1)	74 (27.8)	140 (24.8)		
^a Data available for 17 patients. The incubation period is shown in median and interquartile range.					
Table 2: Clinical characteristics of patients with confirmed monkeypox infection.					

the current outbreak has the potential to push this further. Outbreak containment measures, including vaccines -whenever available-must be aimed at these at-risk populations, but a careful and thoughtful approach must be made to prevent and reduce stigma.

Clinical manifestations of monkeypox contrast between historical and current descriptions. Classically, the disease was divided into prodromal and rash phases, in which fever and lymphadenopathy preceded rash in almost all patients.^{4,5} Skin lesions appeared 1-3 days later, with the face being the most common starting site, and after spreading to other areas.4 In the current outbreak, rash was very common or even, as in our cohort, almost universally present. Interestingly, in our study, a few patients debuted with rash, and about half had a simultaneous appearance of rash and other systemic symptoms. Lesions in the genital or perianal area have been reported in a high proportion of patients, ranging from 36% to 92% in those cared for at sexual health clinics.^{12,16,22,23,27} However, historical reports do not describe lesions in this area, only in the context of a generalized rash.^{4,5} Studies during the Nigerian outbreak were the first to report anogenital lesions, and researchers began hypothesizing about the potential role of sexual transmission.¹⁴ This made PLHIV a population of interest, particularly because some patients were diagnosed with HIV during their medical visit due to monkeypox and were more likely to present with genital lesions.¹⁷ Lesions in the anogenital area were observed in almost half of our study population, more so among PLHIV. Interestingly, we observed a low proportion of proctitis (around 6%), contrasting with almost 40% in other reports, which could be due to underreporting.^{12,16,22,23}

Monkeypox virus is considered to be transmitted via droplets and direct contact with lesions or fomites; the latter being regarded as the predominant mechanism.1,13 In previous studies where some patients were exposed via the bite of an infected animal, only a third of patients developed lesions on the affected site.27 Other outbreaks outside of endemic areas have been mainly linked to contact with lesions of a confirmed case but provide no information on particular sites of touch and subsequent lesion development.15,28 However, the combination of new-onset anogenital lesions and proctitis suggests that inoculation via direct contact has an essential role in spreading the current outbreak. This hypothesis is supported by data from the current and Nigerian outbreaks.12,17 The virus has also been detected in semen of confirmed cases, but the transmission potential of this route is not certain.²⁹ Thus, human monkeypox appears to be transmitted through sexual contact, but care must be taken before properly labelling it as a sexually transmitted condition due to the potential stigmatizing implications this can entail.18

ARTICLE IN PRESS

	Prior HIV diagnosis (%)	No prior HIV diagnosis (%)	All patients (%)	
Number of patients	299 (52.9)	266 (47.1)	565 (100)	
Lymphadenopathies ^a	130 (43.5)	102 (38.3)	232 (41.1)	
Number of affected regions	1 (1-1)	1 (1-1)	1 (1-1)	
Affected regions				
Cervical	54 (18.1)	44 (16.5)	98 (17.3)	
Retroauricular	4 (1.3)	4 (1.5)	8 (1.4)	
Submandibular	5 (1.7)	6 (2.3)	11 (1.9)	
Occipital	0 (0)	1 (0.4)	1 (0.2)	
Axillary	8 (2.7)	6 (2.3)	14 (2.5)	
Inguinal	79 (26.4)	48 (18)	127 (22.5)	
Rash ^b	299 (100)	265 (99.6)	564 (99.8)	
Number of affected regions	3 (2-4)	2 (2-3)	2 (2-3)	
Affected regions				
Scalp	43 (14.4)	31 (11.7)	74 (13.1)	
Face	103 (34.4)	89 (33.5)	192 (34)	
Mouth	24 (8)	18 (6.8)	42 (7.4)	
Neck	32 (10.7)	30 (11.3)	62 (11)	
Chest	137 (45.8)	112 (42.1)	249 (44.1)	
Back	16 (5.4)	12 (4.5)	28 (5)	
Upper limbs	149 (49.8)	130 (48.9)	279 (49.4)	
Hands	8 (2.7)	17 (6.4)	25 (4.4)	
Palms	13 (4.3)	11 (4.1)	24 (4.2)	
Abdomen	47 (15.7)	34 (12.8)	81 (14.3)	
Genital and/or perianal area	171 (57.2)	109 (41)	280 (49.6)	
Lower limbs	116 (38.8)	93 (35)	209 (37)	
Feet	1 (0.3)	6 (2.3)	7 (1.2)	
Soles	14 (4.7)	7 (2.6)	21 (3.7)	
Generalized ^c	10 (3.3)	8 (3)	18 (3.1)	
Skin lesions	_	-	-	
Macules	119 (39.7)	94 (35.3)	213 (37.6)	
Papules	190 (63.5)	142 (53.3)	332 (58.7)	
Vesicles	155 (51.8)	142 (53.3)	297 (52.5)	
Pustules	140 (46.8)	110 (41.3)	250 (44.2)	
Scabs	81 (27)	56 (21.1)	137 (24.2)	
Ulcers	37 (12.3)	21 (7.8)	58 (10.2)	
^a For 27 patients that had lymphadenopathy no specific region was reported. ^b For 35 patients that had rash no specific region was reported. ^c Patients with rash classified as				

"generalized" and in whom no specific region was reported. The number of affected regions is shown in median and interquartile ranges.

Table 3: Characteristics and distribution of rash and lymphadenopathies in confirmed monkeypox cases.

Study limitations

Our study has several limitations. Because the information comes from passive surveillance, cases are not actively sought out in the community. Reporting channels are facilitated as much as possible, but cases may still be missed if patients decide not to look for healthcare, are unable to access care, or if healthcare workers do not report a case. Testing for other diseases that cause rash (such as herpes and varicella) and sexually transmitted infections was not regularly performed. Only in some cases in which monkeypox was negative were such tests performed. Thus, it is likely that a higher number of patients with monkeypox had other infections that could go undetected. Additionally, gender was not documented in the reporting system, only biological sex. Consequently, we could not include a gender-based description. To overcome this, a gender item has already been incorporated in the revised version of the epidemiologic reporting form. Symptoms were not uniformly interrogated for every patient, and documentation of the clinical picture was mostly passive; hence, patients likely provided the most worrisome signs or symptoms, and subtler ones could have inadvertently been ignored. Skin lesions were not assessed in every case by a dermatologist, so misclassification of lesion type could have occurred. However, the document published by the Health Secretariat of Mexico for the management of monkeypox provided examples and

ARTICLE IN PRES

Articles



Fig. 3: Number of symptoms (A), rash (B) and lymphadenopathy regions (C) stratified by HIV status. For 27 patients that had lymphadenopathies and 35 patients with rash, no specific region was reported.

guidance regarding skin lesions, so information bias was likely reduced with this intervention. In part, based on an initial analysis in this report, the Mexican Health Ministry modified a standardized reporting format specifically for monkeypox to improve our understanding of the disease and the epidemiologic response.

In conclusion, the current monkeypox outbreak in Mexico is mainly driven by middle-aged men who have sex with men, of which a large proportion are persons who live with human immunodeficiency virus infection. Containment measures should include spreading trustworthy information about known spread mechanisms and, whenever available, targeting vaccination to groups at higher risk of infection with monkeypox.

Contributors

I.N., M.G.-G., S.E.C.-L., and S.I.V.-F. designed the study. S.E.C.-L., C.T.-S., G.C.-S., G.G.-R., L.S.-L., R.C.-A., A.d.l.T., S.F.-S., and A.Q.-V. acquired the data. I.N. and M.G.-G. performed the data analysis. I.N., M.G.-G., and S.E.C.-L. wrote the first version of the manuscript. H.L.-G., G.R.-T., and S.I.V.-F. revised the manuscript. I.N., M.G.-G., S.E.C.-L., G.G.-R., and S.I.V.-F. had access to all data and vouch for its accuracy.

Data sharing statement

Anonymized data will be made available from the corresponding author upon reasonable request.

Declarations of interests

We declare no competing interests.

Acknowledgements

We thank personnel from the General Directorate of Epidemiology and the Institute of Diagnosis and Epidemiologic Reference for their invaluable work. S.I.V.-F. is supported by the Consejo Nacional de Ciencia y Tecnología (CONACyT) grant A1-S-18342.

Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi. org/10.1016/j.lana.2022.100392.

References

- Titanji B, Tegomoh B, Nematollahi S, Konomos M, Kulkarni PA. Monkeypox - a contemporary review for healthcare professionals. Open Forum Infect Dis. 2022;9(7):ofac310. https://doi.org/10.1093/ ofid/ofac310.
- von Magnus P, Andersen EK, Petersen KB, Birch-Andersen A. 2 A POX-LIKE DISEASE IN CYNOMOLGUS MONKEYS. Acta Pathol Microbiol Scand. 1959;46:156-176.
- Ladnyj D, Ziegler P, Kima E. A human infection caused by mon-3 keypox virus in Basankusu Territory, Democratic Republic of the Congo. Bull World Health Organ. 1972;46:593-597.
- 4 Jezek Z, Szczeniowski M, Paluku KM, Mutombo M. Human monkeypox: clinical features of 282 patients. J Infect Dis. 1987;156(2):293-298.
- Breman JG, Steniowski MV, Zanotto E, Gromyko AI, Arita I. 5 Human monkeypox, 1970-79. Bull World Health Organ. 1980;58(2): 347-353
- Rimoin AW, Kisalu N, Kebela-Ilunga B, et al. Endemic human 6 monkeypox, Democratic Republic of Congo, 2001-2004. Emerg Infect Dis. 2007;13(6):934-937
- Yinka-Ogunleye A, Aruna O, Dalhat M, et al. Outbreak of human 7 monkeypox in Nigeria in 2017-18: a clinical and epidemiological report. Lancet Infect Dis. 2019;19(8):872–879. Erez N, Achdout H, Milrot E, et al. Diagnosis of imported mon-
- 8 keypox, Israel, 2018. Emerg Infect Dis. 2019;25(5):980-983.
- 9 Vaughan A, Aarons E, Astbury J, et al. Two cases of monkeypox imported to the United Kingdom, September 2018. Euro Surveill. 2018;23(38):1800509. https://doi.org/10.2807/1560-7917.ES.2018. 23.38.1800509
- Fang Yong SE, Tek Ng O, Marc Ho ZJ, et al. Imported monkeypox, 10 Singapore. Emerg Infect Dis. 2020;26(8):1826-1830. https://doi.org/ 10.3201/eid2608.191387.
- 2022 Monkeypox outbreak: global trends. World Health Organiza-11 tion. Available at: https://worldhealthorg.shinyapps.io/mpx_global/. Accessed October 10, 2022.

ARTICLE IN PRESS

- 12 Thornhill JP, Barkati S, Walmsley S, et al. Monkeypox virus infection in humans across 16 countries - April-June 2022. N Engl J Med. 2022;387:679–691. https://doi.org/10.1056/NEJMoa2207323.
- 13 GUÍA PARA EL MANEJO MÉDICO DE LOS CASOS DE VIRUELA SÍMICA EN MÉXICO. Secretaría de Salud, Gobierno de México. Available at: https://viruela.salud.gob.mx/docs/2022.07.25_Abordaje ViruelaSimica.pdf. Accessed September 30, 2022.
- 14 Ogoina D, Izibewule JH, Ogunleye A, et al. The 2017 human monkeypox outbreak in Nigeria—report of outbreak experience and response in the Niger Delta University Teaching Hospital, Bayelsa State, Nigeria. *PLoS One*. 2019;14(4):e0214229. https://doi.org/10. 1371/journal.pone.0214229.
- 15 Vaughan A, Aarons E, Astbury J, et al. Human-to-human transmission of monkeypox virus, United Kingdom, October 2018. Emerg Infect Dis. 2020;26(4):782–785. https://doi.org/10.3201/ eid2604.191164.
- 16 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(10353):661–669. https://doi.org/10.1016/ S0140-6736(22)01436-2.
- 17 Ogoina D, Iroezindu M, James HI, et al. Clinical course and outcome of human monkeypox in Nigeria. *Clin Infect Dis.* 2020;71(8):E210–E214. https://doi.org/10.1093/cid/ciaa143.
- 18 Burki T. What does it mean to declare monkeypox a PHEIC? Lancet Infect Dis. 2022;22(9):1286–1287. https://doi.org/10.1016/S1473-3099(22)00540-0.
- 19 Bunge ÉM, Hoet B, Chen L, et al. The changing epidemiology of human monkeypox—a potential threat? A systematic review. *PLoS Negl Trop Dis.* 2022;16(2):e0010141. https://doi.org/10.1371/journal.pntd.0010141.
- 20 Damaso CR. The 2022 monkeypox outbreak alert: who is carrying the burden of emerging infectious disease outbreaks? *Lancet Reg Health Am.* 2022;13:100315. https://doi.org/10.1016/j.lana.2022.100315.

- 21 Tomori O, Ogoina D. Monkeypox: the consequences of neglecting a disease, anywhere. *Science*. 2022;377(6612):1261–1263. https://doi. org/10.1126/science.add3668.
- 22 Girometti N, Byrne R, Bracchi M, et al. Demographic and clinical characteristics of confirmed human monkeypox virus cases in individuals attending a sexual health centre in London, UK: an observational analysis. *Lancet Infect Dis.* 2022;22(9):1321–1328. https://doi.org/10.1016/S1473-3099(22)00411-X.
- 23 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. https://doi.org/10.1136/bmj-2022-072410.
- 24 Ogoina D, Yinka-Ogunleye A. Sexual history of human monkeypox patients seen at a tertiary hospital in Bayelsa, Nigeria. Int J STD AIDS. 2022;33(10):928–932. https://doi.org/10.1177/0956462 4221119335.
- 25 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(32):1018–1022.
- 26 Ogoina D. Sexual behaviours and clinical course of human monkeypox in Spain. Lancet. 2022;400(10353):636–637. https://doi.org/ 10.1016/S0140-6736(22)01497-0.
- 27 Reynolds MG, Yorita KL, Kuehnert MJ, et al. Clinical manifestations of human monkeypox influenced by route of infection. J Infect Dis. 2006;194(6):773–780. https://doi.org/10.1086/505880.
- 28 Reed KD, Melski JW, Beth Graham M, et al. The detection of monkeypox in humans in the Western Hemisphere. N Engl J Med. 2004;350:342–350. https://doi.org/10.1056/NEJMoa032299.
- 29 Lapa D, Carletti F, Mazzotta V, et al. Monkeypox virus isolation from a semen sample collected in the early phase of infection in a patient with prolonged seminal viral shedding. *Lancet Infect Dis.* 2002;22(9):1267–1269. https://doi.org/10.1016/S1473-3099(22) 00513-8.