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Epidemiological and clinical differences of confirmed and discarded Mpox cases on the 2022 Chilean outbreak

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ABSTRACT

Objectives: To improve Mpox diagnosis by identifying distinctive symptoms in confirmed vs discarded cases due to outdated case definition.

Methods: This is a case-control study conducted using data from the Institute of Public Health database, encompassing all suspected cases analyzed by real-time polymerase chain reaction between June 1 and September 30, 2022. We calculated means, frequencies, performed Fisher's test, and computed odds ratios (OR) using RStudio and Microsoft Excel.

Results: Among 1415 suspected Mpox cases, 87% were men aged 30-39 with exanthema. Confirmed cases had higher rates of lymphadenopathy (31% vs 12%), fever (42% vs 29%), myalgia (35% vs 25%), and specific lesions: pustules (36% vs 27%), scabs (25% vs 17%), and umbilicated lesions (24% vs 7%) (P <0.05). Key risk factors for Mpox included contact with a positive case (OR 2.33), multiple sexual partners (OR 3.52), and male gender (OR 29.93).

Conclusion: The symptomatology of confirmed Mpox cases closely aligns with that reported in the current outbreak. The primary risk factors identified include prior contact with another positive case, having multiple sexual partners, and male gender. However, to facilitate a more complete analysis, more evidence needs to be investigated.

Introduction

Mpox is a zoonotic disease belonging to the Orthopoxvirus genus of the Poxviridae family. It was first described during an outbreak in Denmark in 1958 [1,2] and has been recognized as a human disease since 1970, subsequently becoming endemic in central and western Africa [3]. Previous research indicates that its symptoms closely resemble those of smallpox, characterized by multiple skin lesions with various presentations such as macules, papules, vesicles, and pustules, typically located on the palms of the hands or feet [4–8].

Since the outset of May 2022, an unusual surge in Mpox cases has been reported in non-endemic countries, spreading rapidly on a much larger scale than previously recorded [9]. On July 23, 2022, the World Health Organization declared the Mpox outbreak a 'public health emergency of international concern' [10].

Evidence from Europe and North America suggests that the current global outbreak differs in clinical presentation compared to classic Mpox [2]. Specifically, lesions may manifest exclusively in the genital, oral, and perianal regions, without a generalized distribution. In some instances, single lesions have been observed, at times preceding prodromal symptoms or appearing in isolation, and occasionally, lesions may be entirely absent.

Historically, described risk factors included contact with infected animals, as observed during the 2003 outbreak in the United States [11], or sharing personal items such as glasses and towels with confirmed patients [12]. However, recent reports indicate a shift towards person-to-person transmission, potentially even through sexual contact, based on the type and location of lesions documented in this outbreak, which are frequently anal, rectal, or genital [13].

In this outbreak, human-to-human transmission appears to be the primary mode, with frequent genital lesions that could potentially explain infections through sexual contact [13,14].

In Chile, on June 17, the Ministry of Health reported the first confirmed case of Mpox, verified by the Public Health Institute. Nearly a week later, a Health Alert was issued for the country. Our objective is to identify distinguishing symptoms between confirmed and discarded cases to enable a more precise clinical diagnosis and reduce disease transmission.

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Table 1
Definition of cases. A difference is raised between suspicion, which is related to a defined list of symptoms based on historical evidence of the disease, and confirmation based on laboratory results.

Suspected	Confirmed case	Discarded case
Person with a recent onset rash lesion on the skin or mucous membranes (single or simple) and that may present alone or associated with one or more of the following symptoms: fever greater than 38.5°C, chills, myalgias, headaches, lymphadenopathy, low back pain, asthenia, proctitis. Or who also has a history of contact with a confirmed case during the last 21 days.	Person with a molecular diagnostic test (real-time PCR positive for Mpox virus at the ISP or in laboratories defined by Ministry of Health and with authorization from the ISP.	Suspected case with negative real-time PCR and does not meet the definition of a probable case according to the evaluation of the regional health authority.

ISP, Instituto de Salud Pública; PCR, polymerase chain reaction.
Adapted from source: Ministry of Health, Chile.

Methods

Study design and participants

A case-control study was conducted, including all suspected cases as defined in Table 1, who sought medical attention at various health centers. Samples, such as lesion swabs, vesicular content, pustules, or scabs, were analyzed using real-time polymerase chain reaction (PCR) at the Chilean Institute of Public Health (ISP, Spanish acronym for Institute of Public Health).

This study is adapted from the source: Ministry of Health, Chile. The cases include individuals who were suspected patients (as defined in Table 1) and subsequently confirmed for Mpox, whereas the controls encompass all suspected patients who were ruled out for Mpox by PCR testing, during the period from June 1 to September 30, 2022, totaling 1415 cases.

Inclusion criteria were as follows: (1) Individuals residing in Chile meeting the suspected case definition, (2) Cases reported by the health authorities, and (3) Individuals with a 'Positive' or 'Negative' result in the real-time PCR for Mpox. Exclusion criteria included: (1) Cases not officially reported, (2) Cases occurring after September 30, 2022, and (3) Cases with an 'Indeterminate' PCR result.

Data extracted from the notification forms included age, sex, date of sample collection, symptoms, date of symptom onset, type and location of lesions, history of contact with any positive case, date of contact, history of multiple sexual partners, and history of sexually transmitted diseases. Information on smallpox vaccination status was not available.

The dataset used in this study was anonymized, and informed consent was not required, considering the public health significance of the current outbreak and compliance with Chilean legal confidentiality standards.

Procedures

We performed the analysis using Microsoft Office Excel and RStudio (version 2022.02.2). The analysis consisted of two steps: the first involved all suspected cases, and the second compared confirmed cases with discarded cases. We calculated means, percentages, frequencies, and used interquartile ranges or confidence intervals (CI) where applicable. To compare groups, Fisher's test was employed with a significance level set at <0.05. We also calculated odds ratios (OR) with respective confidence intervals and *P*-values <0.05 to assess chances and associations. Logistic regression was used to determine both crude and adjusted OR for associations, with significance set at a 95% CI and *P*-value <0.05 considered statistically significant.

Results

Suspected cases

Between June and September, a total of 1415 patients were classified as suspected cases based on the defined criteria. The first suspected case was reported in epidemiological week 22, and since then, the number of cases has steadily increased, reaching a peak in week 35.

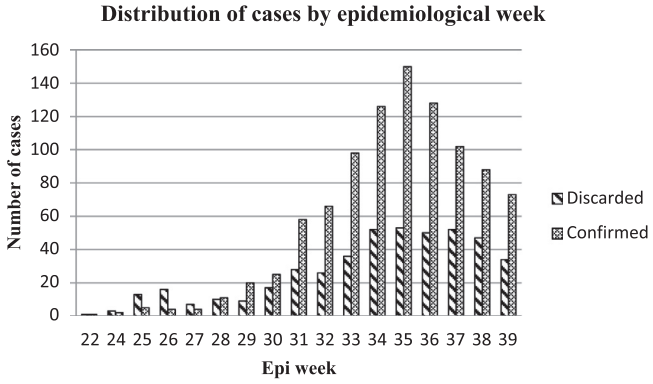

Figure 1. Distribution of suspected cases over time. The positivity of the cases increased as the outbreak progressed until reaching a pick of cases in epi week 35.
Fountain: Database, provided by the Chilean Public Health Institute, June 01, 2022-September 30, 2022. National and Reference Biomedical Department. Subdepartment Viral diseases.

Among the suspected cases, 87% were male, with an average age of 33 years (ranging from 30 to 39 years). Notably, 68% of these cases tested positive for Mpox PCR. Common symptoms among the suspected cases included exanthema (100%), myalgia (68%), and fever (62%). Additionally, 37% of the patients tested positive for some form of sexually transmitted disease, with HIV being the most frequent (36%).

The primary type of lesions reported were maculopapular lesions, typically distributed in the genital area (50%). For a comprehensive overview of the results from suspected cases, please refer to Table 2.

Comparative analysis between confirmed and discarded cases

98% of confirmed cases were males, with a mean age of 35 years. All confirmed cases exhibited skin lesions, and in comparison to discarded cases, they showed higher proportions of lymphadenopathy (31% vs 12%), fever (42% vs 29%), and myalgia (35% vs 25%). These specific symptoms were associated with an increased probability of Mpox occurrence, with OR ranging from 1.65-3.28. Genital and anal areas were the most common sites of lesions. Having multiple sexual partners and contact with a positive case significantly increased the probability of Mpox occurrence, with OR values of 3.52 (CI 2.15-5.80) and 2.33 (CI 1.82-2.98), respectively. A history of sexually transmitted diseases was initially significant but lost significance in multivariate analysis. Being male was the most significant factor in confirming Mpox, with an OR of 20.91 (CI 17.85-50.19). For detailed information, please refer to Tables 2 and 3 and Figure 1.

Discussion

This marks the first outbreak of Mpox in Chile, and our observations align with trends seen in other countries, particularly the concentration of confirmed cases among young men (mean age 35 years, interquartile ranges 28-39 years). This demographic pattern differs from historical ev-

Table 2
Symptoms and characteristics of lesions in suspected, confirmed and discarded cases.

Variable	Suspected case N = 1415	Confirmed Mpox N = 961	Discarded Mpox N = 454	Odd ratio (95% confidence interval)	*P*-value
Age	33 (30-39)	35 (28-39)	31 (22-40)		
Sex (male)	1238 (87%)	943(98%)	295(64%)	29.93(17.85-50.19)	<0.05
Symptoms		N = 961	N = 454		
Fever	878 (62%)	405 (42%)	133 (29%)	1.75 (1.38-2.23)	<0.05
Exanthema	1415 (100%)	961 (100%)	454 (100%)	-	-
Headache	385 (27%)	275 (29%)	111 (24%)	1.23 (0.96-1.59)	0.11
Myalgia	962 (68%)	340 (35%)	114 (25%)	1.63 (1.27-2.10)	<0.05
Back pain	80 (5%)	192 (32%)	64 (28%)	1.55 (0.92-2.63)	0.35
Asthenia	199(14%)	144 (15%)	56 (12%)	1.25 (0.90-1.75)	0.19
Lymphadenopathy	349 (25%)	295 (31%)	54 (12%)	3.28 (2.39-4.50)	<0.05
Rash zone N (%)	N = 1415	N = 599	N = 224		
Face	295 (34%)	219 (36%)	76 (34%)	1.12 (0.81-1.55)	0.50
Sole of feet	84 (10%)	48 (8%)	36 (16%)	0.45 (0.29-0.72)	<0.05
Palm hands	141 (17%)	100 (17%)	41 (18%)	0.89 (0.60-1.34)	0.60
Legs	249 (30%)	178 (30%)	71 (32%)	0.91 (0.65-1.27)	0.61
Arms	284 (34%)	212 (35%)	72 (32%)	1.16 (0.83-1.60)	0.41
Oral cavity	105 (13%)	81 (13%)	24 (11%)	1.30 (0.80-2.11)	0.35
Genital area	411 (50%)	343 (57%)	68 (30%)	3.07 (2.22-4.27)	<0.05
Perianal area	168 (20%)	145 (24%)	23 (10%)	2.79 (1.74-4.47)	<0.05
Chest	245 (30%)	168 (28%)	77 (34%)	0.74 (0.54-1.03)	0.87
Abdomen	227 (27%)	164 (27%)	63 (28%)	0.96 (0.68-1.36)	0.86
Back	257 (31%)	192 (32%)	64 (28%)	1.18 (0.84-1.65)	0.35
Number of lesions N (%)	N = 1415	N = 599	N = 244		
Multiple	577 (70%)	408 (68%)	154 (69%)	1.01 (0.73-1.41)	0.93
Type of lesions N (%)	N = 1415	N = 614	N = 244		
Maculopapular	437(51%)	300 (49%)	139 (57%)	0.72 (0.54-0.97)	<0.05
Vesicular	388 (45%)	278 (45%)	110 (45%)	1.01 (0.75-1.36)	1
Pustule	283 (33%)	220 (36%)	65 (27%)	1.54 (1.11-2.14)	<0.05
Umbilical injury	167 (19%)	150 (24%)	18 (7%)	4.06 (2.43-6.79)	<0.05
Scabs	194 (23%)	154 (25%)	42 (17%)	1.61 (1.10-2.35)	<0.05
Hemorrhagic	13 (1%)	8 (1%)	5 (2%)	0.63 (0.20-1.95)	0.53

Fountain: Database, provided by the Chilean Public Health Institute, June 01, 2022-September 30, 2022. National and Reference Biomedical Department. Subdepartment Viral diseases.

Table 3
Analysis of risk factors. Proportion of suspected cases and a comparison of confirmed and discarded groups with Fisher test, crude OR values and adjusted OR with a multivariate logistic regression.

Variables	Suspected case	Confirmed Mpox	Discarded Mpox	OR (95% confidence interval)			
		n (%)		No adjusted	*P*-value	Adjusted	*P*-value
History of sexually transmitted disease	572 (37%)	391 (41%)	136 (30%)	1.60 (1.26-2.04)	<0.05	1.18 (0.94-1.47)	0.15
HIV	507 (36%)	376 (39%)	131 (29%)	1.58 (1.25-2.02)	<0.05	0.91 (0.73-1.13)	0.41
Syphilis	35 (2%)	22 (2%)	13 (3%)	0.79 (0.40-1.59)	0.52	0.85 (0.72-1.01)	0.07
Hepatitis B virus	7 (0.49%)	5 (0.52%)	2 (0.44%)	1.18 (0.23-6.12)	1	1.05 (0.77-1.44)	0.74
Hepatitis C virus	5 (0.35%)	2 (0.21%)	3 (0.68%)	0.31 (0.05-1.88)	0.39	0.88 (0.61-1.27)	0.5
Sex (male)	1238 (87%)	943 (98%)	295(64%)	29.93(17.85-50.19)	<0.05	20.91 (16.52-40.16)	<0.05
Multiple sexual partners	147 (10%)	128 (14%)	19 (4%)	3.52(2.15-5.80)	<0.05	1.22 (1.10-1.35)	<0.05
Contact with positive case	574 (40%)	443 (48%)	124 (29%)	2.33(1.82-2.98)	<0.05	1.15 (1.10-1.21)	<0.05

OR, odds ratio.
Fountain: Database, provided by the Chilean Public Health Institute, June/01/2022-September/30/2022. National and Reference Biomedical Department. Subdepartment Viral diseases.

idence [3,5,12,15]. However, it is worth noting that the data collection form used did not include questions related to sexual orientation or behavior, preventing a comprehensive comparison from that perspective or other social context inquiries.

Analyzing the clinical presentation, we observe that rash, myalgia, fever, and lymphadenopathy are common prodromal signs among confirmed cases, consistent with reports from various countries. The frequency of these symptoms may vary between reports; for instance, in our analysis, 42% of cases presented fever, which contrasts with frequencies ranging from 62-72% in other studies, and 31% exhibited lymphadenopathy compared to reported frequencies of 57-98% in other countries [14,16].

Interestingly, while headache, back pain, and asthenia are frequently mentioned symptoms, with frequencies ranging from 32-50% of cases in other studies, our analysis did not find statistical significance when comparing the frequencies between confirmed and discarded cases (*P*-value >0.05) [16–20].

In this first outbreak of Mpox in Chile, we have observed several trends that align with reports from other countries. Notably, the majority of confirmed cases are concentrated among young men, which contrasts with historical evidence [3,5,12,15]. It is important to note that our data collection form lacked questions related to sexual orientation or behavior, hindering a more in-depth analysis from that perspective and other social context aspects.

Regarding clinical presentation, we found that rash, myalgia, fever, and lymphadenopathy are common prodromal signs among confirmed cases, consistent with reports from various countries. However, the frequency of these symptoms may vary [14,16]. Symptoms like headache, back pain, and asthenia, although frequently reported in other studies (with frequencies ranging from 32-50%), did not exhibit statistical significance in our analysis when comparing confirmed and discarded cases (P-value >0.05) [16–20].

A similar trend is observed when evaluating the site of the lesion. Lesions in the genital and perianal areas are common among confirmed cases, while lesions on the face, legs, arms, and back, which are reported in many cases worldwide (with frequencies around 30%), lose significance in our study when compared to discarded cases [17,18,20]. It is important to note that there is limited information available detailing the type of lesion, except for one publication from Spain [20], which, similar to our study, indicates maculopapular and pustular lesions as the most frequent among positive cases.

Approximately 48% of confirmed cases reported close contact with another confirmed case, underscoring the importance of investigating close contacts and implementing education initiatives targeted at the at-risk population [12,13,17]. However, it is crucial not to overlook the general population, as the outbreak may continue to evolve, potentially affecting women and children over time.

As in other countries, HIV+ individuals are affected in proportions ranging from 34-57% [17,18,20,21]. In our study, although not statistically significant when analyzed in conjunction with other variables, it remains important to monitor potential coinfections due to the uncertainty surrounding their implications.

Our study has certain limitations, including the lack of smallpox vaccination data in the notification form and the possibility of a non-consulting population, driven by ignorance or fear of stigmatization. Furthermore, as a secondary data study, we encountered missing data that cannot be recovered, potentially introducing biases.

In conclusion, our findings have significant implications for the recognition and definition of Mpox virus cases. Symptoms and lesion locations that differentiate confirmed from discarded cases can guide clinical suspicion and focus quarantine and isolation efforts economically. Nevertheless, everyone meeting the case definition should be tested to contain the spread of the outbreak spread. As more evidence accumulates, a more specific case definition for Mpox can be developed, particularly as epidemiological surveillance becomes crucial over time. Being male, having contact with a previous positive case, and having multiple sexual partners are variables presenting a high probability of Mpox occurrence. Nonetheless, it is essential to remember that many prodromal symptoms and lesion sites may be attributed to other conditions, and this relatively new disease remains both a medical and epidemiological challenge. More comparative studies between confirmed and discarded cases can further strengthen this evidence.

Author contributions

All authors contributed to the study design and data analysis. AA performed the literature review and writing of the article. MG provided critical feedback and contributed to the interpretation of the findings. All authors read and approved the final manuscript.

Declarations of competing interest

The authors have no competing interests to declare.

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Ethical approval

Not required.

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