

Mpox (formerly monkeypox) in women: epidemiological features and clinical characteristics of mpox cases in Spain, April to November 2022

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Over 79,000 confirmed cases of mpox were notified worldwide between May and November 2022, most of them in men who have sex with men. Cases in women, for whom mpox might pose different risks, are rare, and Spain has reported more than one third of those in Europe. Using surveillance data, our study found similar time trends, but differences in delay of diagnosis, sexual transmission and signs and symptoms between men and women.

Over 79,000 confirmed cases of mpox (formerly monkeypox) were notified to the World Health Organization (WHO) between May and November 2022. Most of the cases were notified by previously non-endemic countries in Europe and the Americas. Spain has been one of the most affected countries worldwide, with more than 7,393 confirmed cases [1,2]. The General Director of WHO declared mpox a Public Health Emergency of International Concern (PHEIC) [3] on 23 July 2022. Human-to-human transmission in the context of this PHEIC has primarily been related to close and direct physical contact with skin lesions, crusts or certain body fluids of an infected person, especially in the context of sexual relations, but uncertainties about modes of transmission and the potential impact on general population remain [4-6].

Most cases in Spain and other countries have occurred in men who have sex with men (MSM) [6]. However,

cases in other population groups, such as women, have also been identified. In this study we characterise the mpox cases among women using national surveillance data [7] and explore differences with cases among men to provide information for a better understanding of the disease's dynamics.

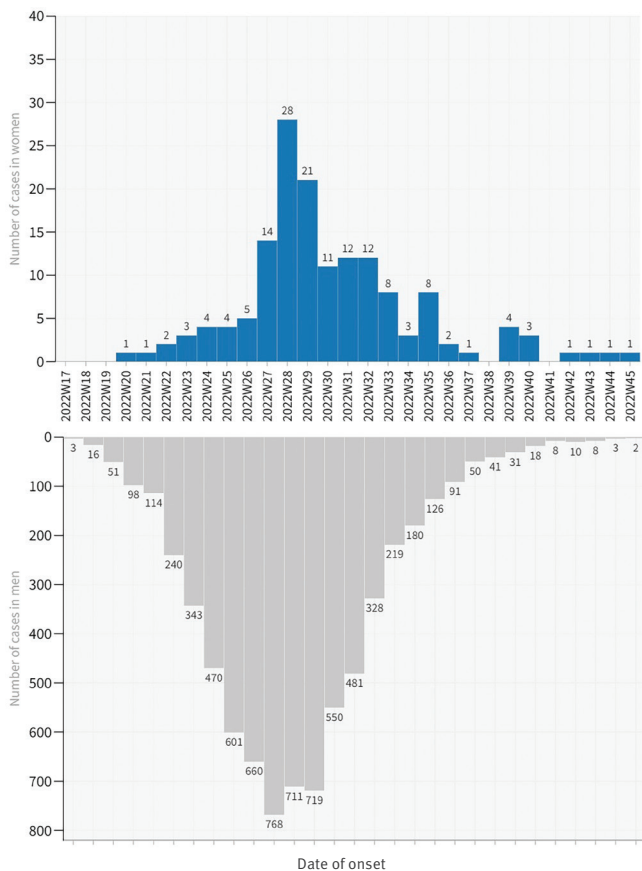
Mpox surveillance in Spain and analysis performed in this study

This analysis includes all confirmed cases (detection of the monkeypox virus (MPXV) genome by specific or generic PCR for Orthopoxvirus in a clinical sample) in Spain that have been collected following the detection and control protocols established by the National Surveillance Network that covers all regions of the country [8]. A standardised form was used by local epidemiologists when interviewing the cases and included sociodemographic variables such as sex (dichotomic man/woman), clinical features and risk factors and exposures.

We conducted a descriptive analysis of the variables included in the form. We excluded all cases younger than 16 years, as the circumstances of the disease in children would require different analysis than those in adults. Comparisons of qualitative variables were studied using the chi-squared test, quantitative variables using the Mann-Whitney U test. Multivariate logistic

FIGURE

Notified mpox cases with known symptom onset, by sex, Spain, 26 April–21 November 2022 (n = 7,091)



regression was performed to adjust measured odds ratio (OR) by sexual transmission mechanism.

Mpox cases in Spanish women

From 26 April to 21 November, 158 mpox cases in adult women (≥ 16 years) were reported in Spain among 7,393 total mpox cases (2.1%). Women (age range: 16–76 years) were younger than men, with a median age of 34 years (interquartile range (IQR): 29–44) vs 37 years (IQR: 31–44) in men. Two women were pregnant.

Evolution of the outbreak and delay in diagnosis

Date of symptom onset of the cases was known for 151 women and 6,940 men. Notified cases showed an increasing trend from April to July (epidemiological weeks 17 to 30), followed by an ongoing decreasing trend (epidemiological weeks 31–46), similar in both women and men (Figure).

Concerning the delay in diagnosis, we found statistically significant differences ($p=0.042$) between sexes. Where information was available (142 women and 6,695 men), the median time from symptom onset to diagnosis was 8 days (IQR: 5–10) in women, compared with 7 days (IQR: 4–10) in men. In hospitalised cases,

we found no significant time differences from symptom onset or date of diagnosis to date of admission.

Sex differences in the mechanism of transmission

The most likely mechanism of transmission was reported for 66.5% of women and 68.0% of men; for both, it was close contact during sexual relationships. However, we found significant differences between men and women with, respectively, 92.9% and 65.7% transmission during close sexual contact ($p<0.001$) (Table 1). A study by Thornhill et al., which categorised women as trans, cis and non-binary, also found sexual contact to be the most likely method of transmission for women, in their sample, in slightly higher percentages [9].

In addition, 14 women (8.9%) were infected in the context of an outbreak linked to a tattoo studio, included in the transmissions group ‘others’, except for a secondary case, who was human-to-human.

In addition, we found differences in the percentage of cases with HIV infection: 4.4% of affected women compared with 40.8% of affected men ($p<0.001$).

Signs and symptoms in women

The most frequent signs and symptoms reported in women were general symptoms, rash in different locations and local lymphadenopathies (Table 2). The combination of signs and symptoms in women was different than in men: women presented anogenital rash less frequently (51.0% vs 67.3%, $p<0.001$) but any rash elsewhere more frequently (71.2% vs 59.1%, $p=0.002$). Men and women had oral exanthema and general symptoms in similar percentages ($p=0.535$ and $p=0.769$, respectively). No differences were found in the number of cases with lymphadenopathies. Differences by sex were still found after adjusting by most probable transmission mode (Table 3).

Higher complication rates were reported in women than in men (14.9% vs 8.8%, $p=0.019$). When comparing specific complications throughout their clinical process, such as secondary bacterial infections, oral ulcers or keratitis, no statistical significance was found. No deaths have been reported in women, while two deaths were reported among the 7,235 men.

Discussion

Cases of mpox reported in women in Spain represent more than one third of all cases in women notified in Europe [10]. During the weeks of increasing incidence in Spain (April to July 2022), cases among women were very rare. However, once the disease spread outside the initial clusters and its incidence was close to its maximum, cases among women followed a similar time distribution as cases among men but at a much lower level. As detected in most countries, the main group at risk are MSM who have high-risk sexual relationships

TABLE 1

Confirmed mpox cases, by sex, Spain, 26 April–21 November 2022 (n = 7,393)

Characteristics	Women (n=158)		Men (n=7,235)		p value
	n	%	n	%	
Median age in years (IQR)	34 (29–44)		37 (31–44)		0.023 ^a
HIV infection ^b	6	4.4	2,682	40.8	<0.001 ^c
Hospitalised ^b	6	4.1	238	3.7	0.767 ^c
Known transmission mechanism	105	66.5	4,918	68.0	0.686^b
Sexual transmission	69	65.7	4,570	92.9	<0.001 ^c
Human-to-human, non-sexual	23	21.9	324	6.6	
Other, not specified	13	12.4	24	0.5	

IQR: interquartile range.

^a Mann–Whitney U test.^b Denominators are the total cases with reported information.^c Chi-squared test.**TABLE 2**

Range of signs and symptoms in mpox cases, by sex, Spain, 26 April–21 November 2022 (n = 7,040)

Signs and symptoms	Women (n = 153)		Men (n = 6,887)		p value ^a
	n	%	n	%	
General symptoms ^b	115	75.2	5,247	76.2	0.769
Anogenital exanthema	78	51.0	4,633	67.3	<0.001
Oral exanthema	26	17.0	1,307	19.0	0.535
Other exanthemas	109	71.2	4,067	59.1	0.002
Local lymphadenopathies	72	47.1	3,432	49.8	0.497
Generalised lymphadenopathies	6	3.9	368	5.3	0.438

^a Chi-squared test.^b Reported any of the following symptoms: asthenia, fever, headache, muscle pain or odynophagia.

[4–6]. Although transmission may happen in other groups, including women, our finding suggests that the monkeypox virus infection has not spread widely to the general population.

One of the main strengths of our study is that we used national surveillance data, including all reported mpox cases in Spain with the early availability of a standardised protocol and an epidemiological form that increased homogeneity of notifications. However, one of the main limitations is the fact that the epidemiological form included, as in all diseases under surveillance in the National Surveillance Network framework, a dichotomous variable for sex, which is a key variable in this analysis. This may have introduced gender misclassification bias in our study. Thornhill et al. classified women as trans, cis and non-binary, finding differences related to gender identity that we could not identify [9], and possibly causing an underestimation of the weight of sexual contact as a method of transmission and the overall risk for women and specifically trans women in our study. In addition, cases were interviewed by many different local epidemiologists, who may have different sensitivity in the information collected for each case. Finally, the number of women among the patients available for analysis was relatively

small, although to our knowledge it is the largest available in literature.

Women were diagnosed later than men, which can be explained by several factors. Given the low-risk perception present in the general population, women may have been less likely to associate their symptoms with mpox, thus delaying consulting and testing. Healthcare practitioners may also introduce gender bias in their clinical suspicion of mpox. Previous authors also described symptoms in women, finding comparable results in the frequency of general symptoms, lymphadenopathies and oral lesions, but higher percentage of anogenital exanthemas and any mucosal exanthemas [9].

HIV prevalence rates in mpox cases were significantly higher than the estimated prevalence of HIV in the adult population in Spain (0.1% in women, 0.6% in men) [11]. This suggests that both men and women with MPXV infection are subgroups with characteristics different from the general population.

As for symptoms, we found in the bivariate analysis statistically significant differences between men and women concerning all non-oral rashes, appearing in different locations, but no differences in general signs

TABLE 3

Odds ratio of signs and symptoms in confirmed mpox cases in women compared with men, adjusted by sexual transmission mechanism, Spain, 26 April–21 November 2022 (n = 7,040)

Signs and symptoms	OR (non-adjusted)		OR (adjusted) ^a	
	OR (95% CI)	p value	OR (95% CI)	p value
General symptoms	0.95 (0.65–1.37)	0.770	0.92 (0.72–1.18)	0.721
Anogenital exanthema	0.51 (0.37–0.70)	<0.001	0.56 (0.45–0.69)	<0.001
Oral exanthema	0.87 (0.57–1.34)	0.530	0.84 (0.39–0.73)	0.725
Other exanthemas	1.72 (1.21–2.45)	0.002	2.20 (1.74–2.77)	<0.001
Local lymphadenopathies	0.89 (0.65–1.23)	0.497	0.97 (0.68–1.39)	0.686
Generalised lymphadenopathies	0.72 (0.32–1.65)	0.417	0.46 (0.25–0.83)	0.009

CI: confidence interval; OR: odds ratio.

^a Multivariate logistic regression was performed to adjust measured OR by transmission mechanism.

and symptoms. These differences remain after adjusting for the transmission mode. Keeping in mind the limitations regarding gender classification previously stated, these differences could be explained by several reasons such as a potential difference in exposures and risks concerning sexual practices (e.g. oral, vaginal and anal sex) that may favour transmission, which is an unknown variable that could not be adjusted for.

Conclusions

To our knowledge, our study describes the largest sample of women with MPXV infection in the available literature. We found that the risk of transmission of mpox in this group exists and must be communicated, although it has remained low throughout the outbreak. Our study provides information relevant to the response to this alert, increasing the knowledge in the disease dynamics in women, and shows how surveillance data can be useful in applied public health research to generate and increase the knowledge about the disease during the outbreak response. Further studies with a more complete classification of sexual orientation and gender identity and the collection of certain risk exposures would help complete the understanding of additional differences in the mechanism of transmission, behaviour and course of the disease in different population groups.

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Ethical statement

Ethics approval was not sought since data was collected by routine surveillance systems, linked to the ongoing multicountry outbreak. No personal identifiable data for case-patients are included in this report.

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Conflict of interest

None declared.

Authors' contributions

BSR, AVP, FRC, VHS, BGH, PSB, LGR, ADF, AGS, MSM, FSS and several members of the National Monkeypox Response Network were part of the response team at the national level. VHS and ADF conceived the idea of the manuscript, and AVP, FRC, BGH drafted the first version of the manuscript in

coordination with BSR with contributions from all authors. All authors, including the National Monkeypox Response Network, have revised the final manuscript.

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Any supplementary material referenced in the article can be found in the online version.

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