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Monkeypox Correlations: Genital Symptoms, Immunocompromised Status and MSM

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ABSTRACT

Objectives: The outbreak of the virus infection Monkeypox (Mpox) in England was on transmission level 2. Mpox and HIV infections may occur simultaneously among the MSM population, exacerbating the symptoms along with treating problems. We aimed to study if Mpox painful genital symptoms correlated with immunocompromised status, sexuality, admissions and length of hospital stay.
Methods: A retrospective data analysis was conducted. The admissions were divided into four groups named: perianal, penile, rectal and other symptoms. Correlations between patients' pain groups, sexuality or immunocompromised status as well as length of hospital stay were studied. Significances were computed by Spearman's rho correlation and Kruskal-Wallis H analyses of variance.
Results: Sixty-nine patients were included, 65 males with mean age=38,5 (SD 8.29; Md=39) and females' mean age=35.5 (SD 9.04; Md= 39.5) years (n.s.). The two gender's Mpox pain areas differed from each other (p= .014). A total of 38% of the male patients presented painful perianal or rectal lesions and 22 males displayed general symptoms and 17 acknowledged MSM. A total of 40% of the males were sexually active with multiple partners; an inverse correlation between males with MSM and males with HIV (rho [25] = -.385*, p= .029, 1-tailed) was revealed. Altogether 23% of males presented HIV and 8% suffered from additional STI. Those with rectal pain had the longest hospital stay with a mean of 6.0 (SD 7.63) days (p= .017) compared to other groups.
Conclusion: Correlations between patients diagnosed with Mpox and genital symptoms were revealed as opposed to inverse correlations between immunocompromised status/HIV and MSM.

Keywords: Monkeypox, anal symptoms, genital symptoms, HIV, MSM

INTRODUCTION

Monkeypox (Mpox), a zoonotic disease, was recognized 1958, in Denmark in von Magnus' laboratory with cynomolgus monkeys used for polio vaccine research (1). The disease has occurred in UK from September 2018 to May 2022 after a person's return from Nigeria. In the end of 2022 verified or probable Mpox cases were estimated to be 2435 in London (2). Momentarily, UK's Mpox transmission is on Level 2, which means that the virus surfaces within a defined sub-population with much tight human contacts (3). Centers for Disease Control (CDC) reports that Mpox spreads besides through intimate tissue contact also from anus, rectum, or vagina (4). Health-care workers' or

household members' first-hand contact leads to advanced transmission (5). Furthermore, zoophilia can trigger Mpox (6).

Past epidemiological data confirmed that 51% of patients carried both Mpox virus and HIV (7) due to sexual contact (8, 9). HIV infection and immunocompromised status may or may not affect the presentation of Mpox. Yet, co-infection of Mpox and HIV can intensify both diseases' symptoms (10). Therefore, the rational of the present paper was to study whether patients with Mpox had correlating symptoms around perianal, penile, rectal or other body areas. Furthermore, we wanted to find out if Mpox correlated with MSM (men having sex with men) or with immunocompromised status / HIV as well as with ways of admission to hospital (elective, non-elective or emergent) as well as with length of hospital stay (LOS).

MATERIAL & METHODS

Sample

A retrospective data analysis for the period from 1st May to 18th September 2022 was performed at a major tertiary UK-hospital for 69 patients (65 males) presenting Mpox. Patients' data included age, gender, sexuality, virus diagnosis, place, date and way of admission to hospital, symptoms, HIV/immunocompromised status and length of hospital stay. The data were collected from September to November 2022 and were accessed for analysis from October 2022 to January 2023. Patients' data were obtained from both online clinical systems and printed medical notes.

Ethical approval was granted before the commencement of this study from the quality improvement and audit department. Registration number: 14986. Consent was waived due to the retrospective nature of the study and data was analysed anonymously.

STATISTICAL ANALYSIS

Data was collected anonymously. Only a research fellow had access to information that could identify individual participants during the data collection period. Data analysis was performed by IBM SPSS version 26. ANOVA and One sample t-tests were used to test significance between several independent variables in the same sample. For two independent groups, t-tests were applied when considered appropriate. Non-parametric tests: Mann-Whitney U-test, Spearman rho correlations and multivariate Kruskal-Wallis H analyses of variance adjusted for ties, were used.

RESULT

Age and Mpox transmission:

This study included 69 patients presenting Mpox at the departments for Infectious disease, General medicine and a centre Specialized for HIV patients. The 65 males' mean age was 38,52 (SD 8.29; Md=39) and 4 females' mean age was 35.5 (SD 9.04; Md= 39.5) years (n.s.). The sample's age ranged from 22-59 years (Table 1). A total of 66 patients were subject to human-to-human transmission in UK and 3 males knew that they had been exposed to confirmed Mpox as well as 3 males got infection from travel abroad.

Mpox and symptoms

By ANOVA a difference was revealed between the two gender's four problematic Mpox painful areas: perianal, penile, rectal and other pains ($F[3,61]= p= .014$), females had solely other pains (Fig.1). Yet, rectal pain and penile oedema were the most common presentations that required hospital admission. Also, males had lesions or pain in other body areas, that is, in mouth, nose, eye, face and finger (Fig.1). The group with 'other pains' suffered from lesions more so than the perianal-pain group ($t[27]=3.45$; $p= .002$).

Mpox and lesions

A total of 26/69 (38 %) patients had lesions in the reproductive organs, 23/69 (33%) did not have such problems and 19/69 (28%) had lesions or pain in other body areas. The distribution of lesions was not the same across the 4 pain groups (Kruskal-Wallis

[KW] H= 10.27 [df=3] = p= .016). Comorbidity between males (mean 2.41 (SD 1.94) and females 1.75 (SD 1.5) was n.s. (Fig. 1, Table 1, 2).

Table 1. The patients' length of hospital stays correlated with pain, care centre and comorbidity

VARIABLES	N	RHO MEAN (SD)	PAIN RHO	RHO; P≤
LESION X PAIN	63	1.81 (0.78)	.406	.002**
LOS = LENGTH OF HOSPITAL STAY X PAIN	69	4.42 (5.77)	.286	.028*
PAIN GROUP X LOS	67	2.48 (1.16)	.394	.001**
CARE CENTRE X LOS	69	1.35 (0.61)	.334	.005**
COMORBIDITY X LOS	69	2.38 (1.92)	.447	.001**

Note. Spearman's rho**. Correlation is significant at the 0.01 level (2-tailed); *Correlation is significant at the 0.05 level (2-tailed)

Table 2. Differences between patients' length of hospital stay, pain groups, way of admission and care centre.

VARIABLES	M/F	N	MEAN	TEST	P≤
GENDER & AGE: MALES	M	65	38.5	t= .483	n.s.
FEMALES	F	4	35.5	(df=67)	
LOS = LENGTH OF HOSPITAL STAY	M	61	4.25	t= 2.295	.029*
	F	4	9.75	(df=39)	
PAIN GROUPS: 1 PERIANAL, 2 PENILE, 3 RECTAL & 4 OTHER PAINS	M	61	2.38	t= 11.238	
	F	4	4.00	(df=60)	.001**
ADMISSION: ELECTIVE	1	15	1.93	Kruskal-Wallis	
NON-ELECTIVE	2	12	2.33	H=11.154	
EMERGENCY	3	40	2.72	(df=2)	.004**
CARE CENTRE: INFECTIOUS DISEASE	1	50	2.47	Kruskal-Wallis	
GENERAL MEDICINE	2	14	2.43	H= 7.844	.002**
HIV SPECIALISED CENTRE	3	5	2.75	(df=2)	

Note **t-test is significant at the 0.01 level (2-tailed). Kruskal-Wallis H analysis of variance between 3 groups ** H is significant at the 0.01 level.

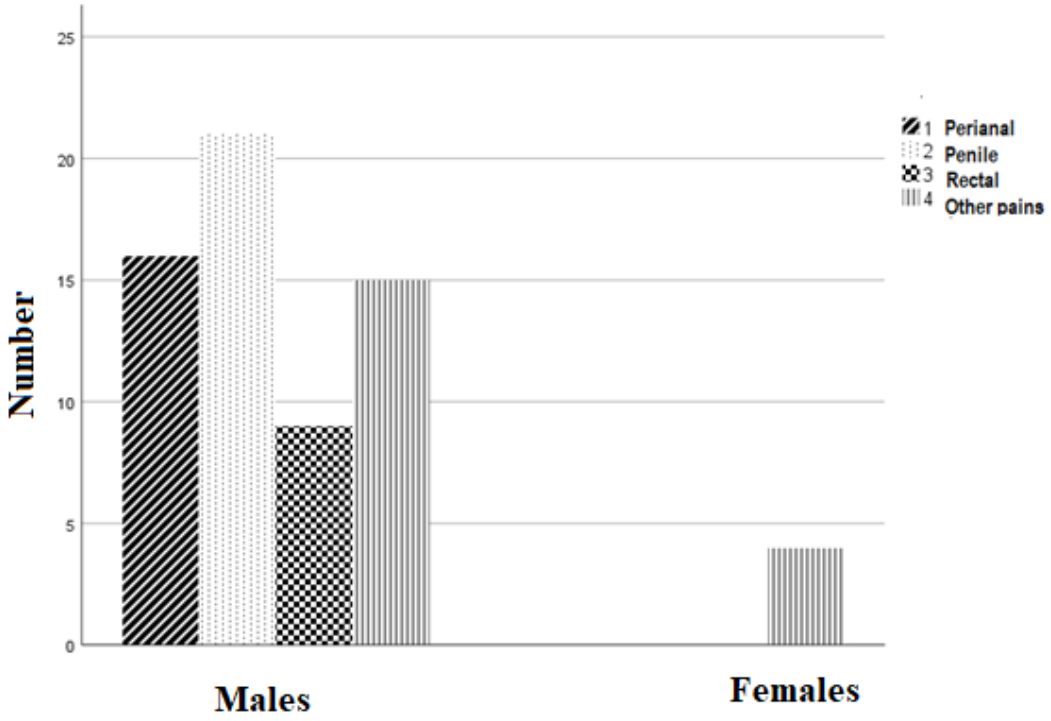

Figure 1. Males' and females' pain

Mpox and sexuality

A total of 10/25 (40%) of the males were sexually active with multiple partners. Furthermore, there was an inverse correlation between males with MSM and males with HIV (rho [25] = -.385, p= .029, 1-tailed). Altogether 15/65 (23%) males presented HIV and 5 (8%) suffered from additional sexually transmitted infections (STI) such as chlamydia, gonococcal infection and lymphogranuloma venereum [LGV] proctitis, gonorrhea and syphilis. Between males with HIV and antiretroviral therapy (ART) a good correlation was revealed (rho [25] = .667; p = .000, 2-tailed).

Mpox and immunosuppression:

Between males with both Mpox and MSM an inverse correlation with immunosuppression was found (rho [24] = -.356, p= .044, 1-tailed).

Mpox and admission to hospital

Patients' way of admission to hospital could be elective, non-elective or emergent; 9% were admitted electively, 17% were admitted non-electively and the major part of patients 71% were admitted in emergency. Two patients arrived with attenders. Females arrived more urgently than males (t[64]= 4.191, p=.001). The hospital admission way correlated with the perianal, penile and rectal pains (rho 431, p= .002, 2-tailed), i.e., more pain led to more emergent admission; yet, way of admission correlated inversely with having lesions (rho [63] = -.299, p= .017, 2-tailed).

Mpox and length of hospital stay

Females had a longer hospital stay than male patients (Table 1, 2). Length of hospital stay correlated with the perianal, penile and rectal pains, (rho = 286, p =.028; 2-tailed). A closer look revealed that the penile-pain group had the shortest hospital stay with a mean of 1.6 (SD 3.69) day as opposed to the rectal-pain group with the longest hospital stay with a mean of 6.0 (SD 7.63) days (KW H= 13.711, SD 2.77, p= .017). Also, between the care-centres: Infectious disease, General medicine and HIV-specialized centre a significant difference was found as regards patients' length of stay at hospital. (KW H= 7.227, df=63, p=.027 adjusted for ties). Altogether 72.5% of the patients were cared for under Infectious disease (range 0-25 days), 20.3% were cared for in General medicine unit (range 0-14 days) and 7.2% cared for in the HIV-specialized centre (range 2-7 days), (Table 1, 2).

DISCUSSION

Mpox and phylogenesis

If Mpox transmission from animal to human is suspected, animal health authorities must be informed for future research collaboration (11). Mpox virus' phylogenesis has been divided into Clade I (earlier named 'Central African' with severe outcomes), Clade IIa (earlier 'West African clade' from imported animals), and Clade IIb (presently at hand and other genomes). All UK genomes fell into Clade IIb in 2022 (3). UK had in November 2022 a total of 3507 verified and 149 possible Mpox cases but no reported death (12).

Mpox and age

In UK, 3730 verified Mpox cases were revealed in the beginning of 2023 (13). Altogether 98.6 % males, and 1.4% females were at hand. The median (Md) age of the UK Mpox cases was 37 years and belonged to the same age group our sample fitted into with a Md 39 years (14)

Mpox and symptoms

Four Mpox pain areas: perianal, penile, rectal and other pains were revealed in males. Rectal pain and penile oedema were the most common presentations requiring hospital admission. Yet, a fifth of the males had lesions or pain in other body areas. The distribution of lesions differed across the 4 pain groups. A total of 38 % of the patients had lesions in the genitals, in accordance with Patel et al.'s findings that patients with Mpox presented with mucocutaneous

lesions, most commonly on the genitals (n=111 participants, 56.3%) or in the perianal area (n=82, 41.6%) (15). Rectal pain and penile oedema are symptoms that are not currently included in public health messaging. However, clinicians must think about Mpox infection in patients presenting such symptoms. The unconventional development of temporal lesions should lead the clinician to considerate Mpox infection.

Mpox and sex

Past research indicated from a sample of 54709 Mpox cases that the majority lived as MSM (16). In UK, Mpox cases were related to networks of gay, bisexual, and MSM people; yet, there are also some infected females mainly due to sexual contact. Our results did not agree with the statements that MSM had been disproportionately infected by Mpox (17). In contrast, we found an inverse correlation between males with both Mpox and MSM and those with immunosuppression.

Mpox and HIV

People living with HIV are subject to a greater hospitalization rate for Mpox as opposed to those HIV negative. The link between Mpox severity and untreated HIV indicates that to reduce Mpox, people need to know their HIV status and to have access to ART to achieve viral suppression. Considerable co-morbidity exists in patients with Mpox infection, along with severe pain and complications due to secondary bacterial infection (3). We found that 23% males presented with HIV and 8% had additional STI.

Mpox and admission

In our sample the admission way to hospital was emergent for 71 % of our patients. The clinical presentation of female cases is known to include fever, lymphadenopathy, oropharyngeal and genital lesions. The range of clinical diseases in female patients comprises severe manifestations, with an estimated 4 cases requiring admissions to hospital for managing Mpox related symptoms (3) in agreement with our 4 admitted females with Mpox.

Mpox and hospitalization

A meta-analysis (18) included 7540 Mpox cases out of which 7.4% were hospitalized. Altogether 15 deaths took place and 7 occurred in the Central African Republic (CAR) during a period of two months (Dec. 2015-Jan. 2016). The remaining eight deaths were recorded between 2017 and 2019 in Nigeria. The case-hospitalization rate (CHR) was estimated to be 14.1% (7.3–27.0) and the case fatality rate (CFR) was projected to be 0.03%, with large citation heterogeneity in the meta-analysis (18).

Mpox and its elimination

UK's current goal is elimination of Mpox. The term "elimination" denotes implementing transmission on Level 1 instead of currently being on Level 2. Level 2 suggests a transmission within a defined population group. (19) As long as Mpox transmission is on Level 2, there is a feasible increase in healthcare utilization. Quick infection detection reduces the CHR and CFR (18). WHO recommends restriction of number of sex partners and avoidance of sex with unfamiliar individuals as 3 of the male patients were infected abroad, then among other things, guidance on travel restrictions is needed (20).

Limitation of the study and future directions

The availability of demographic and retrospective Mpox data of a sample of 69 patients save costs and time. Therefore, use of retrospective data is attractive (21); but may comprise lower level of evidence compared with prospective studies. Namely, a convenience sampling is not necessarily characteristic for the general population. To minimize biases, multivariate analysis is recommended, and we followed this recommendation in the present study. For future research we suggest that a prospective multicentered

study with standardized questionnaires for relevant information is performed on Mpox-suspected patients. Those patients who do not get Mpox can then serve as controls.

CONCLUSION

Correlations between patients diagnosed with Mpox and their genital symptoms were observed as opposed to inverse correlations between immunocompromised status/HIV and MSM. The group with rectal-pain had the longest hospital stay.

List of abbreviations:
Mpox: Monkeypox
HIV: human immunodeficiency virus
ART: antiretroviral therapy
CDC: Centers for Disease Control
WHO: World Health Organisation
MSM: men having sex with men
STI: sexually transmitted infection
CHR: Case-hospitalization rate
CFR: Case fatality rate

Declaration by Authors

Ethical Approval: Approved
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