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An Epidemiological and Clinical Study of Monkeypox in Changsha, China: A Retrospective Analysis of HIV-Infected and Non-HIV-Infected Patients from June to December 2023

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Background: The World Health Organization (WHO) declared Human Monkeypox (mpox) as a public health emergency of international concern (PHEIC) in July 2022. Due to border quarantine and isolation measures implemented from January 2020 to December 2022, Beijing did not report its first locally transmitted case of mpox until May 31, 2023, which represented a delayed occurrence compared to other countries. The aim of this observational analysis is to describe demographical data, symptoms presentation and clinical course till outcome of patients diagnosed with monkeypox (mpox) from June to December 2023 at a tertiary level hospital in Changsha, china.

Patients and Methods: We conducted a retrospective study on 44 confirmed mpox cases and compared laboratory data between HIV-infected and non-HIV-infected patients at a tertiary general hospital in Changsha, China.

Results: All patients were male, with a median age of 33 years. 88.6% patients had sex with men (MSM), and 88.9% HIV-infected patients accepted antiretroviral therapy (ART). The early symptoms of mpox typically include rashes and fever, which usually appear around the penis or anus. There were significant differences were found between HIV-infected and non-HIV-infected patients in laboratory data ($P < 0.05$), but none were clinically significant.

Conclusion: This study underscores the importance of targeted mpox management strategies in MSM populations, particularly those co-infected with HIV and syphilis. Health authorities should consider proactive prevention and control measures, especially given the overlapping epidemics of HIV, syphilis, and mpox. Further studies are needed to explore the long-term clinical outcomes and potential benefits of vaccination in preventing mpox among high-risk populations.

Keywords: Monkeypox virus, HIV, Syphilis, MSM, Rash

Introduction

Mpox, formerly known as human monkeypox, is a zoonotic disease caused by the mpox virus (MPXV), an enveloped, double-stranded DNA virus of the *Orthopoxvirus* genus of the *Poxviridae* family.[1] To date, three phylogenetically distinct

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clades of Monkeypox Virus (MPXV) have been identified. The "Central African" or "Congo Basin" clade is referred to as clade I, while the "West(ern) African" clade encompasses clades II and III.[2] The virus was first diagnosed in a 9-month-old boy from the Democratic Republic of the Congo (DRC) in 1970.[1] Clade II was responsible for the first outbreak of mpox outside Africa, which occurred in the United States in 2003.[1] In September 2017, another outbreak was identified in Nigeria.[1] Subsequently, on May 6, 2022, a United Kingdom national returning from Nigeria was diagnosed with mpox after developing a febrile rash.[1] This marked the beginning of the 2022 outbreak, which spread to non-endemic countries worldwide.[2–5] The World Health Organization (WHO) declared it as a Public Health Emergency of International Concern (PHEIC) in July 2022, which was later lifted on May 11, 2023.[6] Between January 1st, 2022, and September 30th, 2024, a cumulative total of 109,699 laboratory-confirmed cases of MPXV infection, accompanied by 236 fatalities, were reported in 123 Member States across all six WHO regions.[6] Owing to variations in medical resource allocation, epidemic prevention measures, and societal behaviors, the epidemiological and clinical features of mpox cases exhibit differences between Asia and Europe/America.[3,5,7] Notably, up to 99% of all cases reported during this outbreak were in homosexual, bisexual, and other men who have sex with men.[1] According to WHO report, China is one of the ten countries which are the most severely affected mpox.[6] In September 2022, China reported the first imported case of mpox.[8] While the global mpox outbreak began spreading rapidly in Europe and North America in 2022, China, due to the border quarantine and isolation measures implemented for inbound travellers in response to the coronavirus disease 2019 (COVID-19) pandemic from January 2020 to December 2022, did not report its first local case of mpox until May 31, 2023. This delay in occurrence was in contrast to other countries.[9] In June 2023, Changsha, an inland city in China, reported the first confirmed case of mpox. The First Hospital of Changsha has been the designated hospital as the treatment facility for mpox in the Changsha area from June to December 2023. We conducted a comprehensive study to analyze the epidemiological and clinical features of laboratory-confirmed mpox patients in the Changsha area from June to December 2023. The key point is on identifying demographic and clinical distinctions between HIV-infected and non-HIV-infected patients.

Material and Methods

Study Objects

In this retrospective study, we enrolled all consecutive patients who tested positive of the MPXV through nucleic acid testing and diagnosed with mpox from June to December 2023, at the First Hospital of Changsha, a tertiary general hospital in China. All patients conformed to the diagnostic criteria for confirmed cases as outlined in the Technical Guidelines for Mpox Prevention and Control (2022 edition) developed by the National Health Commission of China. We excluded patients whose medical records are severely missing. Mpox patients who completed study period were finally analyzed as shown in Figure 1.

Methods

Definition of confirmed mpox cases: A. Individuals who exhibit similar mpox symptoms, such as an unexplained acute rash on the face, oral mucosa, limbs, genitals, perineum, perianal area, etc., accompanied by a fever (>37.3 °C) or lymphadenopathy. B. Individuals who have had any of the following epidemiological histories within 21 days prior to onset: a. Travel history to areas with reported mpox cases; b. History of contact with confirmed or suspected mpox cases; c. History of engaging in same-sex sexual activity, or having a same-sex sexual activity; d. History of suspected animal contact in endemic areas. C. Individuals who have tested positive for MPXV nucleic acid or virus isolation in the laboratory. Confirmed cases must meet all three of the above criteria.

When encountering individuals with symptoms suggestive of mpox, infectious disease doctors collected oropharyngeal and vesicular or pustular fluid swabs from all individuals and sent them to the laboratory of the Changsha Center for Disease Prevention and Control for virus nucleic acid testing. The laboratory used a specific RT-PCR test provided by Jiangsu Bioperfectus Technologies Co., Ltd. (Jiangsu, China) to confirm the presence of mpox virus DNA. A positive result was determined if the Cycle Threshold (CT) value of the RT-PCR was ≤ 37. Blood samples were collected from patients and subjected to routine blood cell analysis and biochemical testing in the laboratory of the First hospital of

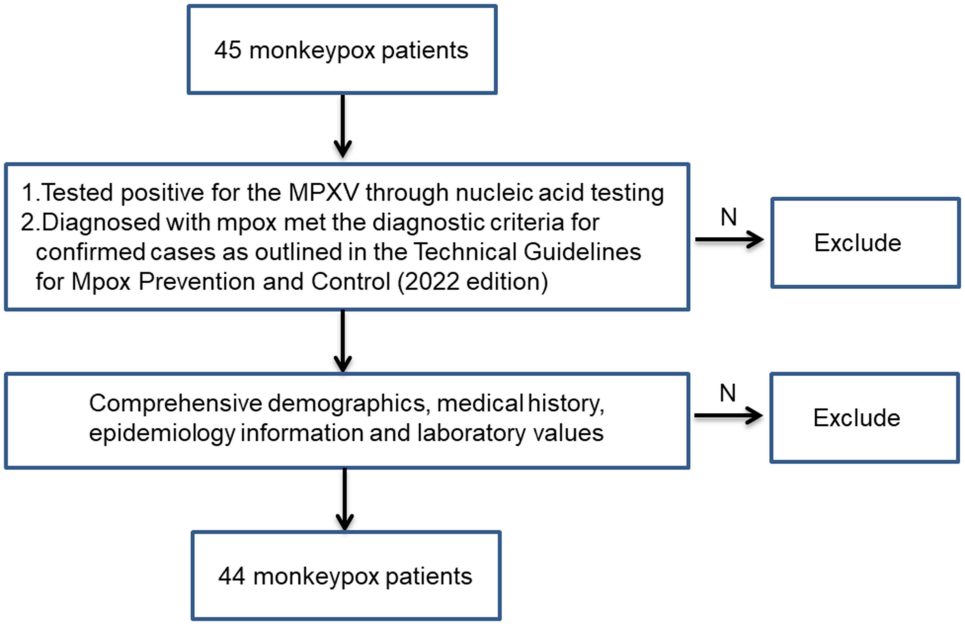

Figure 1 Case collection process diagram.

Changsha. To rule out the possibility of coexisting sexually transmitted infections (STIs), we also conducted serology tests for HIV, syphilis, and hepatitis. For people living with HIV (PLWH), we evaluated the most recent CD4+ count (cells/mm^3) and HIV viral load within the six months preceding mpox diagnosis, disease course, and antiretroviral therapy (ART).

Upon identifying a case of illness, infectious disease doctors conducted an epidemiological investigation on the patient. They gathered a diverse range of information, encompassing demographic specifics, clinical symptoms prior to diagnosis, medical background, exposure history within the past 21 days preceding the onset of illness, and close contacts from four days before the illness began until the time of diagnosis. Utilizing a standardized case report form, they acquired demographic, epidemiological, clinical presentation, laboratory, and clinical outcome data.

The following data were obtained from the hospital information system: demographic factors (age, gender, occupation, sexual orientation, marital status), HIV status, syphilis infection status, other comorbidities, epidemiological risk of exposure (high-risk exposure, exposure to a confirmed mpox case, and/or travel to an endemic area in the past 21 days), length of hospital stay, clinical presentation, medication, laboratory data, superficial lymph node ultrasound results, complications and clinical outcomes.

This study was conducted in accordance with all relevant tenets of the Declaration of Helsinki and approved by the Medical Ethics Committee of the First Hospital of Changsha (China)(Approval Number: 2022–220) without the need of written informed consents. The data were extracted from the routine clinical records and transferred to an anonymised, password-protected database, which was securely maintained and not contained personally identifiable information.

Statistical Analysis

The data were initially recorded in Microsoft Word and subsequently summarised in Microsoft Excel to create a database. Following the auditing process, the data were imported into the SPSS 25.0 statistical package for statistical verification, collation and analysis. The frequencies and proportions were reported for categorical variables, as well as the medians and interquartile ranges (IQR) for continuous variables. Normally distributed data were analysed using one-way ANOVA with mean ± standard deviation (X ± s) representing the results, while non-normally distributed data were tested using non-parametric tests, represented by Median (IQR), and intergroup comparisons were tested using Mann–Whitney *U*-test. When the P-value is less than 0.05, the difference is considered statistically significant.

Results

Demographics and Clinical Characteristics

A total of 44 cases of mpox were diagnosed and included in this observational study. Table 1 presents the baseline characteristics of all cases. All cases were young male, with a median age of 33 (IQR 19, 54) years old, who self-identified as homosexual or bisexual (67.5%). 6 patients (13.6%) had been vaccinated against smallpox during childhood, as smallpox vaccination was compulsory in China until 1981. Among the 44 patients, 39(88.6%) of them were men who had sex with men (MSM) and reported having had a sexual encounter 21 days before the consultation date. No patients had travelled abroad during the previous month. In these patients, the mean time elapsed between the last reported sexual intercourse and the onset of symptoms was 5.9 ± 2.8 days, with a median time between the beginning of symptoms and medical examination of 6.9 days, with an interquartile range of 4.0 to 9.5 days. The majority of these patients have

Table 1 Demographics, Medical History, Epidemiology Information and Laboratory Values Among Confirmed Mpox Cases of Changsha, China from June to December 2023[($\bar{x}\pm$ s)/N(%)]

Variables	N = 44
Age (years)	33(19,54)
Male [N (%)]	44(100)
Homosexual or bisexual [N (%)]	27(61.4)
History of smallpox vaccination [N (%)]	6(13.6)
Epidemiological link	
MSM [N (%)]	39(88.6)
Close contact with mpox cases [N (%)]	1(2.3)
Incubation period (days)	5.9±2.8
Time between beginning of symptoms and medical examination (days)	6.9(4.0,9.5)
Concurrent infection	
HIV-positive [N (%)]	27(61.4)
Syphilis infections [N (%)]	28(54.5)
Initial laboratory data	
White blood cell count ($\times10^9\cdot L^{-1}$)	6.96±1.46
Neutrophil count ($\times10^9\cdot L^{-1}$)*	3.87±1.18
Lymphocyte count ($\times10^9\cdot L^{-1}$)	2.35±1.02
Monocyte count ($\times10^9\cdot L^{-1}$)	0.51±0.19
Platelets count ($\times10^9\cdot L^{-1}$)	203.02±58.94
Red blood cell count ($\times10^{12}\cdot L^{-1}$)	4.62(4.42,5.00)
Hemoglobin (g/L)	145.00(138.00,148.00)
Total protein (g/L)	68.29±5.03
Albumin (g/L)	38.15(37.12,41.35)
Alanine aminotransferase (U/L)	23.35(16.35,30.95)
Aspartate aminotransferase (U/L)	19.95(16.20,26.75)
Total bilirubin (μmol/L)	11.06±4.14
Lactate dehydrogenase (U/L)	221.50(198.00,241.50)
Creatinine (μmol/L)	75.52±14.43
Creatine kinase (U/L)	84.25(68.85,122.80)
Creatine kinase isoenzyme-MB (U/L)	14.95(11.20,23.40)
Procalcitonin (ng/mL)	0.06(0.03,0.11)
C-reactive protein (mg/L)	17.68(11.25,31.20)
Outcomes	
Length of hospital stay (days)	10.51(7.15,13.91)
Death [N (%)]	2(4.5%)

Abbreviation: MSM, men who have sex with men.

Table 2 Laboratory Values in PLWH Diagnosed with Mpox [($\bar{x}\pm$ s)/N(%)]

Variables	N = 27
Standardized Antiretroviral Therapy [N (%)]	24(88.9)
Newly diagnosed [N (%)]	2(7.4)
HIV RNA < 20 copies·mL^{-1} [N (%)]	16(59.3)
Course of disease (years)	5.0(3.5,8.0)
CD4<200 cells·mm^{-3} [N (%)]	4(1.48)

coexisting infections, including human immunodeficiency virus (HIV) (27/44, 61.4%) or syphilis (28/44, 54.5%), with 21 patients suffering from both conditions simultaneously.

Among the 27 patients with a diagnosis of mpox and HIV infection (Table 2), 24 (88.9%) received standardised antiretroviral therapy. Of the 24 patients with recent test results, 16 exhibited undetectable HIV levels, while 8 exhibited a viral load of >20 copies·mL^{-1}. With regard to the CD4+ cell count, four patients exhibited a count of <200 cells·mm^{-3}, while three patients did not provide this information. Both deceased patients were HIV-positive and had not vaccinated against smallpox, with one of them being newly diagnosed with HIV.

Clinical Presentation

In this group of mpox cases, all patients with mpox exhibited symptomatic. The most prevalent early symptoms were rash and fever. The most common symptoms related to mpox were rash(44, 100%), genital lesions(34, 77.3%), fever (27, 61.4%), anal lesions(19, 43.2%), skin lesions(18, 40.9%)and lymphadenopathy (10, 22.7%). Figure 2 provides a summary of the clinical presentation of mpox in all 44 patients. In this group of cases of mpox, the rash initially appeared as papules and gradually transformed into herpes, with a diameter of approximately 0.4 to 1 cm. The rash typically began on penis (26, 59.1%) or perianal region (11, 25.0%), and gradually spread to head, face, chest, back, limbs, palms, and soles of the feet. The rash could be observed to progress through different stages in different parts of these patients' body (Table 3).

In this group of cases, the laboratory findings were characterized by increased levels slightly of lactate dehydrogenase, with a median value of 221.5U/L (IQR 198.00, 241.50), and C-reactive protein, with a median value of 17.68 mg/L (IQR 11.25, 31.20). There were statistically significant differences in neutrophil count, red blood cell count, albumin, aspartate aminotransferase, total bilirubin, and creatine kinase isoenzyme MB between HIV-infected and non-HIV-infected patients diagnosed with mpox ($P < 0.05$) (Table 4), though these differences were of no clinical significance.

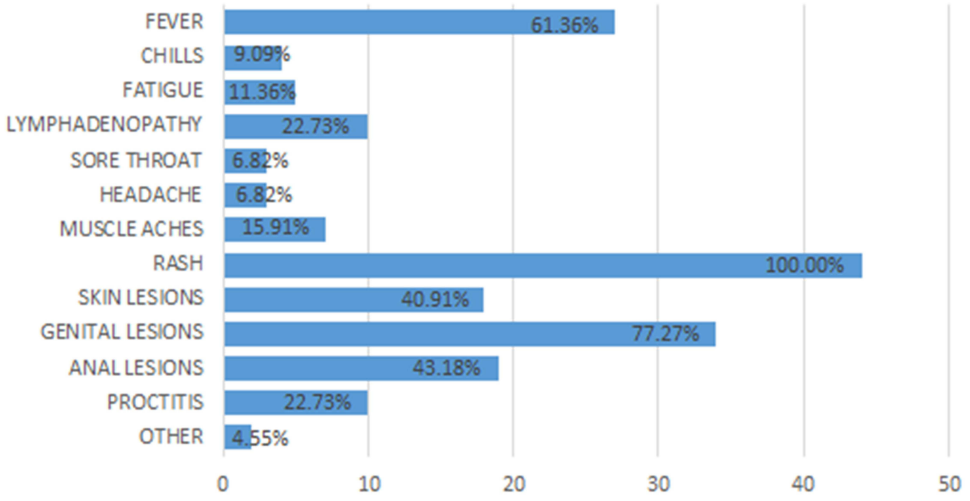

Figure 2 The most common symptoms related to mpox.

Table 3 Distribution of Initial Sites of Rash and Rash Sites in 44 Monkeypox Patients [N(%)]

Anatomical sites	Initial rash sites (%)	Subsequent rash sites (%)
Penis	26(59.1)	34(77.3)
Perianal region	11(25.0)	19(43.2)
Head and/or face	3(6.8)	23(52.3)
Human limbs	2(4.5)	23(52.3)
Chest and/or back	1(2.3)	17(38.6)
Belly	0	8(18.2)
Palm	0	12(27.3)
Foot	0	2(4.5)

Table 4 Comparison of Laboratory Data in HIV-Infected versus HIV-Uninfected Patients Diagnosed with Mpox ($\bar{x}\pm s$)

Variables	HIV-infected (n=27)	HIV-uninfected (n=17)	*P* value
White blood cell count ($\times10^9\cdot L^{-1}$)	7.40(6.37,8.03)	6.73(5.45,7.71)	0.17
Neutrophil count ($\times10^9\cdot L^{-1}$)*	4.12(3.31,4.91)	3.30(2.53,4.18)	**0.02**
Lymphocyte count ($\times10^9\cdot L^{-1}$)	2.13(1.42,2.83)	2.43(1.91,3.41)	0.33
Monocyte count ($\times10^9\cdot L^{-1}$)	0.50(0.40,0.60)	0.51(0.31,0.63)	0.99
Platelets count ($\times10^9\cdot L^{-1}$)	197.00(166.00,248.50)	180.00(155.00,217.00)	0.35
Red blood cell count ($\times10^{12}\cdot L^{-1}$)*	4.46(4.32,4.77)	4.91(4.65,5.02)	**0.00**
Hemoglobin (g/L)	142.00(132.00,147.00)	146.00(141.00,150.00)	0.08
Total protein (g/L)	69.30(64.05,71.90)	67.30(65.50,70.20)	0.65
Albumin (g/L)*	37.60(36.95,39.95)	39.60(38.20,41.80)	**0.01**
Alanine aminotransferase (U/L)	23.20(15.60,27.65)	24.30(19.60,43.60)	0.23
Aspartate aminotransferase (U/L)*	18.80(15.50,22.50)	25.00(17.30,31.60)	**0.04**
Total bilirubin (μmol/L)*	8.60(6.45,11.30)	12.30(11.10,15.30)	**0.00**
Lactate dehydrogenase (U/L)	216.00(196.50,235.00)	230.00(202.00,251.00)	0.33
Creatinine (μmol/L)	72.10(65.15,82.40)	75.90(73.20,80.20)	0.24
Creatine kinase (U/L)	80.10(66.15,126.15)	92.10(69.50,117.20)	0.60
Creatine kinase isoenzyme-MB (U/L)*	19.10(12.10,40.70)	12.00(10.20,13.60)	**0.00**
Procalcitonin (ng/mL)	0.05(0.04,0.10)	0.09(0.03,0.16)	0.83
C-reactive protein (mg/L)	21.70(12.15,39.65)	13.60(10.90,22.40)	0.06

Notes: *p value <0.05 was considered statistically significant.

Most patients just received supportive treatment and only one patient purchased cidofovir by himself due to the impact of the accessibility of anti-monkeypox virus drugs. Of the 44 cases, the prevalent secondary complications were bacterial skin and soft tissue infections (14, 31.8%) and proctitis (10, 22.7%), followed by pharyngitis (8, 18.2%) and keratitis (3, 6.8%). Among these cases, seven patients presented with mixed infections, and one patient developed secondary sepsis. Twenty-one patients received antibacterial drug, comprising beta-lactam agents such as cefuroxime and ceftriaxone, as well as quinolone drugs including levofloxacin and moxifloxacin.

Discussion

This observational study provides a comprehensive overview on the clinical features, epidemiological characteristics and laboratory findings of 44 patients with mpox, whom observed in the second half of 2023 in the inland Chinese city —— Changsha.

To begin with, these cases presented a later outbreak of mpox and a lower incidence of severe cases in this region which compared to European and American countries.[2–5,10–12] This may be attributed to the implementation of isolation

measures against novel coronaviruses in mainland China, resulting in a delay in the spread of the MPXV in mainland China, and consequently, a lower incidence of severe epidemics.[7,9,13]

Moreover, these cases were predominantly young and middle-aged males, the majority of patients had sex with men (MSM) prior to the onset of the disease, which is consistent with previous reports.[11,14,15] The majority of patients were co-infected with HIV or syphilis, indicating that the disease is prevalent in patients with compromised immune systems. The mean incubation period was approximately 5.9 days, with cases necessitating hospitalisation for 4.0–9.5 days from the onset of the disease. The overall hospitalisation period was relatively brief, and the prognosis was favourable based on the administration of symptomatic supportive treatment.

Thirdly, it was observed that approximately two-thirds of the patients in this group had previously been diagnosed with HIV infection. This suggests that the mpox is relatively common in patients with weakened immune systems. Furthermore, the majority of patients had been treated with ART, which did not appear to reduce the risk of mpox virus transmission. It is pertinent to note that two patients with HIV and syphilis co-infection died in this group of cases. A comparable situation has been documented in Nigeria,[16] whereas no deaths have been previously reported in Europe.[2,4] Our analysis indicates that there is no evidence to suggest an association between HIV and mpox. A similar perspective has been previously documented.[11,17]

Rash and fever were commonly reported as early symptoms of mpox in this group, consistent with findings from similar studies conducted in the United Kingdom, Spain, Italy, the United States, and other countries.[2,4,5,16,18] Rashes typically manifested around the penis or anus initially, and were also observed on the extremities, face, and trunk. These findings were consistent with those of previous studies and indicated a correlation with MSM.[2,4,5,16,18]

Results of this study demonstrated that lactate dehydrogenase and C-reactive protein levels were slightly elevated in all patients, while the white blood cell count, lymphocyte count, platelet count, alanine aminotransferase, and albumin levels remained within the normal range. Furthermore, although there were several differences in the laboratory data between mpox patients with HIV infection and without HIV infection, these differences had no clinical significance.

A paucity of literature exists on peripheral blood laboratory findings in patients with mpox. Elevated levels of C-reactive protein have been reported in patients with mpox in laboratory tests.[15,19] It may be related to the fact that the patients included in this study were young and middle-aged and less likely to present with severe clinical manifestations. Moreover, it may be related to the fact that MPXV inhibits the ability of CD4+T and CD8+T lymphocytes to recognise mpox-infected monocytes, which does not have the ability to attack and destroy lymphocytes. Furthermore, it may also be a degree of immune escape, resulting in fewer inflammatory cytokines being released.

The 2022 edition of China's Technical Guidelines for Mpox Prevention and Control states that the current treatment of mpox is primarily symptomatic supportive therapy, with the aim of alleviating symptoms, preventing and controlling complications, reducing morbidity and mortality. In this group of cases, patients exhibited mild conditions and less severe complications, who received mainly symptomatic supportive treatment, as well as antibiotic treatment for secondary skin and soft tissue infections and proctitis. The majority of patients had a favourable prognosis. Comparing the most recent WHO data on the global mpox outbreak, the case fatality rate outside the African region was 0.19%.[6] It was observed that patients with mpox and HIV co-infection, exhibiting a CD4+ T lymphocyte count of less than 200 cells/mL, tend to present with more severe clinical manifestations. In case of severe illness, these patients may ultimately succumb to the disease.[12] In this group, two patients with severe disease and a combined HIV and syphilis infection had a CD4+ T lymphocyte count of less than 200 cells/mL. Further observation is required to ascertain whether patients with combined HIV infection who do not receive ART and have CD4+ T lymphocyte counts below 200 cells/mL will present with severe disease.

In this study, even though 6 patients were vaccinated against smallpox when they were young, they were still diagnosed with mpox. The median age of the subjects was greater than 45 years, which indicating that following this period of immune maturation, antibodies capable of neutralising smallpox viruses may have gradually lost their capacity to provide cross-protection. The current smallpox therapeutics and vaccines are cross-reactive with MPXV.[14,20] Nevertheless, the therapeutic efficacy of various therapeutic and vaccine products against mpox is limited, and the development of specific therapeutics and vaccines against mpox is still required. Therefore, it is recommended that the

development of antiviral drugs targeting the replication steps of the viral life cycle that can inhibit viral replication independent of viral entry.[21]

The limitations of this study include a relatively small sample size and patients only in Changsha region, which lead to potential biases in data collection. In the epidemiological investigation of this study, some patients may have provided inaccurate information regarding their sexual exposure, which has resulted in inaccurate calculations regarding the incubation period and the inability to ascertain the presence of asymptomatic infections with MPXV. In addition, longitudinal follow-up on patients to assess long-term effects and complications are lack. To broaden mpox understanding, multi-center studies with large samples across regions are crucial. Follow-up studies on asymptomatic cases using serological testing are needed. Further research should focus on immune response mechanisms to MPXV in HIV co-infected patients. Efficacy of treatments and new antiviral drugs targeting MPXV should be investigated. Longitudinal studies are essential for insights into long-term outcomes and CD4+ T lymphocyte counts' relationship with disease severity. Enhanced data collection methods and collaboration with public health authorities are key for monitoring outbreaks, assessing prevention strategies, and informing future responses.

Conclusions

Similarly to other international cohorts, MPXV primarily infects the MSM population. Among the patients diagnosed with mpox, the most prevalent clinical manifestations were rash and fever. The initial presentation of rash was frequently observed on the genital region, with the potential for subsequent development on the face, trunk, and limbs. This combination of symptoms offers a valuable opportunity for the early identification of mpox patients and the timely implementation of isolation measures when coupled with the distinctive presentation of herpes. Despite biases related to sample size and patient reporting, our study offers clinical doctors crucial insights and guidance for early diagnosis and management of suspected mpox in MSM populations. Moreover, it suggests targeted interventions for public health practitioners to adopt for the MSM population, encompassing nucleic acid testing and vaccination. Further studies are needed to explore the long-term clinical outcomes and potential benefits of vaccination in preventing mpox among high-risk populations. This study contributes to the improvement of health workers' understanding of the mpox and provides a reference point for future prevention, control and research.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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