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Case Series

Clinical Spectrum and Evolution of PCR-Confirmed Monkeypox: A Case Series of 6 Patients

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Abstract

Background The zoonotic orthopoxvirus illness Monkeypox (Mpox) is re-emerging. While historically characterized by a particular course of symptoms, current outbreaks have revealed a range of clinical signs and symptoms, particularly in terms of the onset of lesions as well as systemic prodrome

Objective To explain the clinical characteristics, particular dermatological progression patterns as well as results of 6 patients with PCR confirmed Mpox to help doctors in early identification.

Methods This case series was conducted at Department of Dermatology, Combined Military Hospital (CMH) Lahore, where patients who tested positive for Mpox Virus by Polymerase Chain Reaction (PCR) presenting between December 1, 2025 and January 31, 2026, were incorporated in the study. The data collected as well as analyzed included demographics, traveling history, sexual history, prodromal symptoms as well as lesion morphology, primary site, progression and clinical resolution.

Results Primary lesions appeared in the genital and supra - pubic areas of all 6 male patients (mean age 27.1 years) in crops. Only 33 % (n=2) experienced fever before rash onset, indicating atypical prodromes. Inguinal lymphadenopathy was associated in 100% of cases (n=6), which was noteworthy. Over an average of 9 days, the lesions progressed from papulovesicular to typical umbilicated pustules with central crusting. Within 2.8 to 4 weeks, full clinical resolution had been attained.

Conclusion The present global outbreak of Mpox is characterized by a "genital-first" pattern and highly variable prodromal symptoms, as evidenced by this particular case series. The 100% presence of inguinal lymphadenopathy within our cohort is a crucial diagnostic indicator, particularly when conventional symptoms such as pre-rash fever are not present. Clinicians must maintain a low index of suspicion and a low threshold for PCR assessment when encountering localized genital crops, irrespective of traveling history or febrile condition of the patient.

Keywords Monkeypox; Mpox; Genital rash; Inguinal lymphadenopathy; Orthopoxvirus.

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Introduction

Monkeypox (Mpox) is a viral zoonotic disease brought on by the monkeypox virus, a fellow member of the Orthopoxvirus genus.[1] Historically endemic in West and central Africa, the virus has recently seen worldwide dissemination, prompting the world Health Organization (WHO) to declare it a public health concern.[2] The classical medical picture described in historic literature involves a unique febrile prodrome followed by lesions at first on face and trunk, consequently spreading in a centrifugal

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pattern and associated lymphadenopathy.[3] While historic data from endemic areas showed Mpox being largely a pediatric disease, the 2022-24 global outbreaks have revealed a remarkable predilection for sexual transmission among adult networks.[4,5] Current epidemiological shifts suggest evolving transmission characteristics. Consequently, medical presentations have become increasingly varied, often mimicking common sexually transmitted infections (STIs).[6]

Clinicians in non endemic regions face difficulties in differentiating Mpox from many other vesiculopustular eruptions. The lack of "textbook" symptoms - like the absence fever before rash, can result in missed or even delayed diagnoses.[7] This particular case series describes the medical characteristics, dermatological progression patterns, along with results of 6 individuals with PCR confirmed Mpox presenting to tertiary care center in Pakistan. The target is to highlight atypical presentations to facilitate early isolation and management.

Methods

This case series was conducted at Department of Dermatology, Combined Military Hospital (CMH) Lahore. We incorporated patients who presented between December 1, 2025 and January 31,2026.

Patients of every age or gender with a clinically suspicious rash (vesicular, pustular, ulcerated or umbilicated lesions) who afterwards tested positive for Monkeypox Virus by Polymerase Chain Reaction (PCR) were incorporated. PCR confirmation was performed utilizing lesion swabs (after deroofing vesicle/ pustule or from ulcer) sent to Armed Forces Institute of Pathology, Rawalpindi.

Individuals with negative PCR were excluded from the study.

Patients were assessed through detailed history and examination, which included demographic information such as age, gender, travel history (both international and domestic), prodromal symptoms such as fever, headache, myalgia, and sore throat, lesion chronology (site of onset, spread pattern), morphological development and presence of lymphadenopathy.

All patients provided Informed consent for publication of the clinical data, and case series was approved by the ethical review board committee CMH, Lahore vide reference No. 783/2026.

Result

The detailed clinical characteristics of all six patients are summarized in **Table 1**.

Six male patients (mean age 27.1 years) with PCR-confirmed Mpox were included in this case series. The clinical data differs from the usual textbook explanation. Fifty percent of the cohort reported recent travel and one patient reported transactional sexual contact 15 days prior to onset of rash. The remaining 50% reported no travel or sexual history, suggesting localized community transmission **(Figure 1)**.

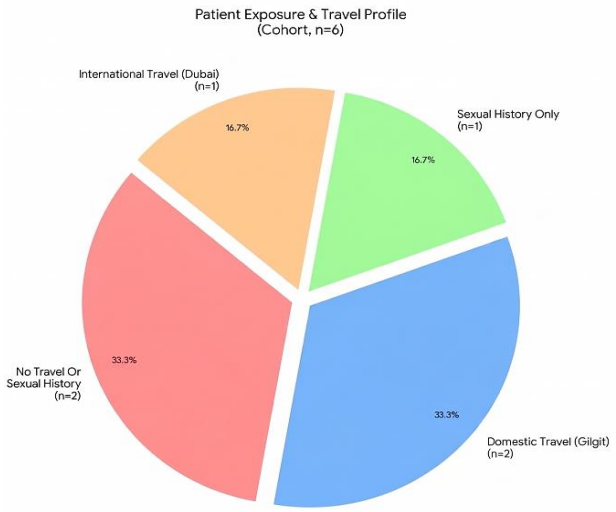

Figure 1 Presumed primary mode of exposure is either through sexual contact or travel, with figure demonstrating percentages of patients with either domestic/international travel or having sexual contact. Patients with no travel or sexual history also given in percentage.

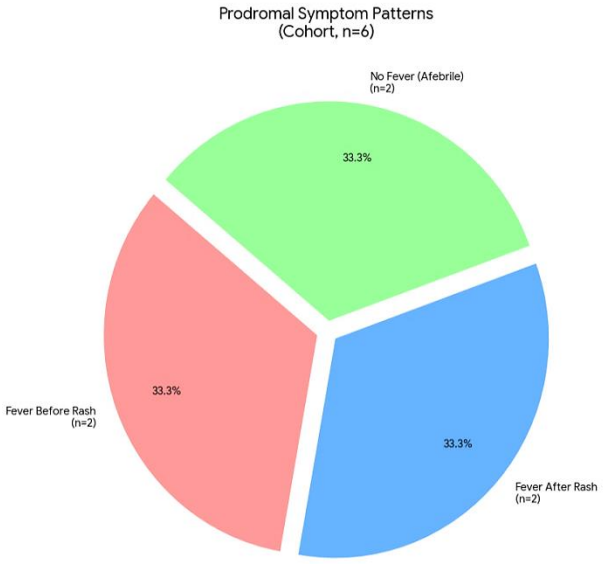

Figure 2 Shows patients with no prodromal features, fever before rash and fever after rash in cohort of 6 patients

Among the striking clinical findings was the inconsistency of systemic prodrome; only 33% (n=2) had fever before rash. Most people did not develop a fever after the rash (n=2) or were completely afebrile (n=2) **(Figure 2)**.

Patient 5 had a "lymphadenopathy-first" phenotype where painful inguinal swelling preceded all other symptoms. Despite this systemic variability, the inguinal lymphadenopathy was a universal clinical marker (100%), frequently with secondary nodal involvement of the cervical (50%) or axillary (16%) chains. Primary lesions appeared as "crops" localized to the genital, inguinal, and supra-pubic areas. Morphologically, it took an average of 9 days for the disease to spread centrifugally to the head, face, limbs, and oral mucosa (tongue) from the papulovesicular stage to characteristic umbilicated pustules with central brown or black crusting. Screening for co-infections was comprehensive, and 100% of the cohort was tested negative for HIV, VDRL, and TPHA. All cases achieved full clinical resolution within 2.8 to 4 weeks **(Figure 3)**.

Discussion

This case series illustrates the significant variability

Table1 Clinical Characteristics of Mpox Patients; Shows Primary lesion site, Progression of rash to different body areas , Changes in morphology with time, Different lymph nodes involvement, Presence of other sexually transmitted diseases.

Variable	*Patient 1*	*Patient 2*	*Patient 3*	*Patient 4*	*Patient 5*	*Patient 6*
Primary Lesion Site	Inguinal & Supra-pubic	Base and Shaft of penis	Inguinal & Supra-pubic	Shaft of Penis	Shaft of Penis & Supra-pubic	Supra-pubic region
Rash Progression	Supra-pubic → Hands → Face → Head → Feet (Progression in 9 days)	Genitalia → Chest/Abdomen → Head → Face (Progression in 8 days)	Inguinal → Supra-pubic → Back → Legs → Head (Progression in 10 days)	Genitalia → Face → Head → Limbs/hands (Progression in 10 days)	Genitalia → Trunk → Tongue → Head → Limbs (Progression in 8 days)	Supra-pubic → Legs → Trunk (Progression in 9 days)
Morphology	Papule → Pustule → Umbilicated with central brown crusting	Papule → Vesicle → Pustule → Umbilicated with central black/brown crusting	Umbilicated papules → Central brown crusting	Papule → Vesicle → Umbilicated with crust	Papule → Vesicle → Pustule → Umbilicated with central brown crust	Vesicle → Pustules with surrounding erythema → Umbilicated with central brown crust
Lymphadenopathy	Bilateral Inguinal (Palpable & Tender)	Bilateral Inguinal, Right posterior Cervical (Palpable)	Left inguinal (Palpable)	Left Inguinal, B/L Posterior Cervical (Palpable)	B/L Inguinal, B/L posterior Cervical, Right Axillary (Palpable)	Right Inguinal (Palpable & Tender)
Other STDs (HIV, VDRL, TPHA)	Negative	Negative	Negative	Negative	Negative	Negative

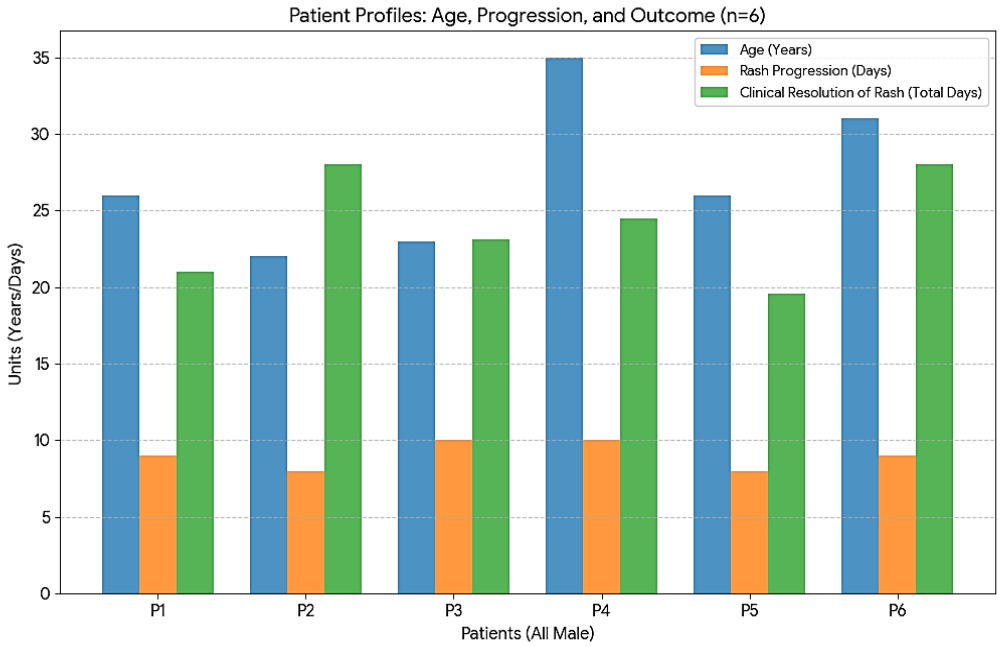

Figure 3 Patients' age (in years), progression of rash (in days) and resolution of rash (in days).

in the clinical presentation of Mpox in the current outbreak context, reinforcing findings from recent global studies.[8] A striking finding in our series is that all six patients presented with initial lesions in the genital, inguinal, or supra-pubic region **(Figures 4D, 5B, 6B, 7D, 8 and 9)**. This contrasts with the classical description where the rash typically begins on the face **(Figure 9)**.[9] The rash progression data in **Table 1** clearly demonstrates a pattern of "Genital Centrifugal" spread. This pattern strongly suggests that the primary site of inoculation was via intimate or sexual contact, aligning with data from the 2022 multi-country outbreak reported by Thornhill *et al*;[10] however only one patient gave history of sexual contact. The systemic prodrome was highly inconsistent in our cohort, with only 33% (n=2) of patients experiencing prodromal symptoms before the rash appeared. Two patients (Patients 3 and 5) remained afebrile during the initial stages, while Patients 4 and 6 developed fever only after the lesions surfaced. This total absence of fever, observed in 33.33% of our cases, highlights a significant shift in the clinical phenotype of the current Clade IIb outbreak.

We follow the trend of Patel *et al*. (2022) in which 13.7% had no systemic symptoms and 38.5% had a rash as the first symptom.[11] Fever preceded the rash in 34% of cases, according to Ogoina *et al*.[12]

Figure 4 Patient 1; A-C shows papular lesion on face, hands and foot on day 3 of presentation; D shows centrally umbilicated lesions with central brown to black crusting on day 9 of rash onset.

Figure 5 Patient 2; A) papules on dorsum of hand of on day 8 of presentation; B) centrally umbilicated lesions with central black to brown crust on day 8 of rash onset.

Figure 6 Patients 3; A) crusted papule on head on day 8; B) umbilicated lesions with central black to brown crust of on day 10 of rash onset.

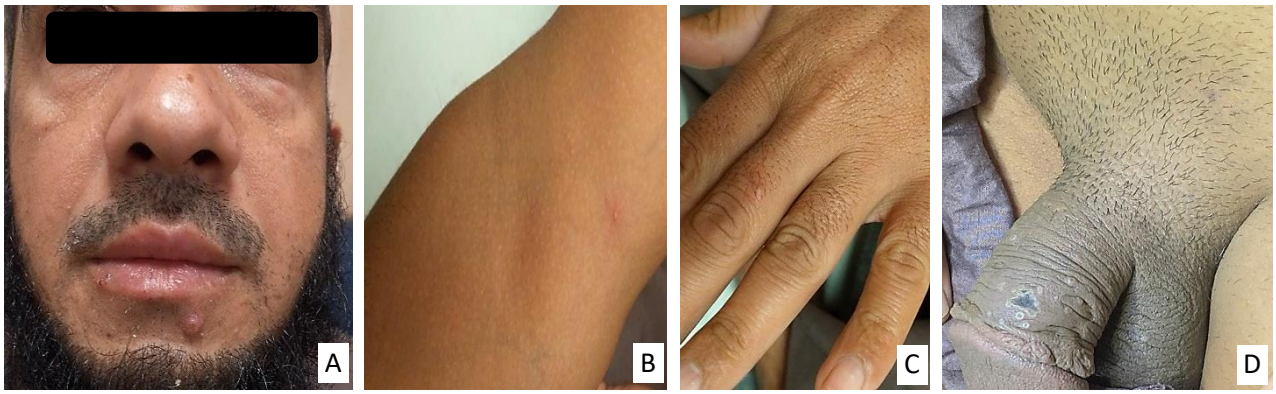

Figure 7 Patient 4; A-D showing lesions on face, arm, hand, genitalia on day7.

Figure 8 Patient 5 centrally umbilicated papules on abdomen and black crusted umbilicated lesions on base of genitalia on day 8.

Figure 9 Patient 6 pustules with surrounding erythema right inguinal and pubic area on day 6.

Our data confirms that 66% of our cohort were afebrile or developed fever later in the disease course. Thus, there is a need to move away from fever-based triage by keeping a lower threshold for PCR testing in patients with new-onset genital crops and lymphadenopathy. Lymphadenopathy is still a major clinical differentiator between Mpox and other vesiculopustular eruptions like Varicella.[6] As noted by Bayer-Gner in 2005, histological features of viral infections overlap but the clinical markers like lymphadenopathy differentiate Mpox from smallpox and varicella-zoster virus.[13] Palpable inguinal lymphadenopathy was seen in 100% of patients (n=6) in this series. This correlates well with the genital and supra-pubic findings which use surrounding lymph nodes for drainage. Half of the cohort (n=3) were specifically tender upon palpation (Patient 1, 5, and 6). Our data is not limited to localized inguinal involvement. Large systemic lymphatic engagement occurred with 50% of the posterior cervical lymph nodes involvement and patient 5 presenting with involvement of the right axillary medial group. Our series has a higher prevalence of inguinal lymphadenopathy (100%),

than reported in some larger international cohorts, for example, in Thornhill *et al*, making it a better-defined marker for clinicians evaluating genital crops in current outbreak.[4] As shown in Titanji *et al*. (2022), atypical afebrile presentations in 66% of our cohort warrant a shift in triage away from fever to sentinel markers like inguinal lymphadenopathy to avoid missed diagnosis during clinical screening.[14]

Conclusion

Vesiculopustular rashes, especially those that show up as localized crops in the supra-pubic and genital regions, must remain the primary differential diagnosis of Monkeypox.

The current outbreak is characterized by a progression from the suprapubic and genital area to the extremities, as evidenced by our findings. To avoid missed diagnoses as well as additional community, awareness of afebrile presentations as well as sentinel markers is crucial.

Limitations Despite the significant clinical insights provided, this study is limited by its small sample size and data gathered from a single tertiary care center in Pakistan. Due to social stigma, proper travel and sexual history may have social desirability bias. Consequently, larger multi-center studies are required to validate these atypical "genital-first" presentations across broader populations

Declaration of patient consent Authors certify that they have obtained all appropriate patient consent.

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Conflict of interest No conflict of interest.

Author's contribution

FS: Have made substantial contributions to conception and design, acquisition of data, analysis and interpretation of data and drafting the manuscript.

QUDK: Have made substantial contributions to conception and design and revising the manuscript critically.

MN: Have made substantial contributions to conception and design and drafting the manuscript.

KH: Substantial contribution to data analysis and interpretation of data, critical review of the manuscript.

MK, UN: Have made substantial contributions to acquisition of data and revising the manuscript critically.

TS: Have made substantial contributions to analysis and interpretation of data and revising the manuscript critically.

Every author has given final approval of the manuscript version to be published and agreed to be accountable for all aspects of the work.

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