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Correspondence

Clinical characteristics of human monkeypox laboratory confirmed cases: Lessons from observational studies

Dear editor,

Monkeypox is a zoonotic double-stranded DNA virus belonging to the *Poxviridae* family (*Chordopoxvirinae* subfamily) that is closely related to the smallpox virus, but generally less severe than smallpox [1]. There are two genetic clades of this virus: West African and Central African [2].

The first case reported is related to a 9-month old child in the Democratic Republic of Congo (DRC) in 1970, where smallpox had been eradicated [3]. Since that time, the virus has been endemic in most West and Central African countries. The first outbreak outside of Africa was in 2003, involving pets imported into the United States. That outbreak was exclusively related to animal-to-human transmission [4,5]. Human to human transmission was initially limited to the central clade, which is more severe than the western clade both in mortality and morbidity.

Nevertheless, some significant reports showed human to human transmission in the Central African Republic (CAR), Democratic Republic of Congo (DRC), South Sudan, and Nigeria [6]. Along with COVID-19 pandemic, an outbreak of human monkeypox in the United Kingdom and other European and non-European Union countries with more than two thousand cases have been reported up to June 21, 2022, have been reported [7]. Hypothesis on behavioral changes of the virus implies possible sexual transmission. Spread to other countries and increased middle-aged involvement raise concerns about human monkeypox as a global concern [6–8].

The virus is detected in samples taken from almost all body fluids (such as serum, plasma, saliva, urine, semen and vaginal fluids). In addition, samples obtained from anogenital regions are positive for MPXV DNA in real-time PCR [9]. There is evidence to raise suspicion over sexual transmission and transmission through skin to skin and mucosal contact [10]. The virus appears to be most prevalent among homosexuals (MSM). Attention to education and disease awareness becomes important for control and prevention, especially in LGBT and MSM populations who may be sexually active [8].

Historically, human monkeypox has been regarded to be an endemic disease circulating in highly endemic areas. However, sporadic cases in non-African countries indicate that the disease is no longer confined to the previously endemic areas. Therefore, regarding the limitation of previous studies, we investigated its characteristics and manifestations for better patient management and establishment of accurate control programs.

After a comprehensive search of the literature, we found eight relevant observational studies evaluating the clinical aspects of individuals infected with human monkeypox [9–16]. This article is based on data from 1280 laboratory confirmed human monkeypox patients. Our results suggested that human monkeypox mostly affected male gender (79.3%; 95%CI: 56.2–91.9), especially in men who had sex with men (MSM) (79.8%; 95%CI: 76.1–83.0). The median age of the infected cases was 35.3 years, with a positive seroprevalence for HIV in about 40.4% (95%CI: 16.3–70.3).

The prevalence of human monkeypox among those with multiple sexual partners was 32.0% (95%CI: 4–98.3). From 1280 confirmed cases, the prevalence of monkeypox in at-risk populations such as health-care workers, family in contact with a confirmed case, and inmates in the same prison was 3.3% (95%CI: 1.2–8.4), 58% (95%CI: 48.1–67.3), and 33% (95%CI: 24.5–42.8), respectively, with a median day from onset to first contact of approximately 12 days. 18% (95%CI: 11.6–26.8) of the confirmed cases had no prodromal symptoms.

The re-emergence of monkeypox was associated with concomitant sexually transmitted diseases. Our findings showed that the prevalence of concurrent STD was 60.2% (95% CI: 5.7–97.4), including syphilis 43.2% (95% CI: 9.2–85.1), herpes simplex virus (HSV) 44.4% (95% CI: 31.9–57.8), chlamydial infections 10% (95% CI: 5.5–17.6) and gonococcal infections 15% (95% CI: 9.2–23.4).

Based on the initial medical consultations, frequent clinical symptoms were rash (97.2%; 95%CI: 58.9–99.9), fever (75.4%; 95%CI: 54.5–88.7), headache (79%; 95%CI: 69.9–85.9), pruritus (73%; 95%CI: 63.5–80.8), lymphadenopathy (38.6%; 95%CI: 7.9–82.1), myalgia (63.0%; 95%CI: 53.2–71.9), sore throat (39.7; 95%CI: 17.3–67.5), fatigue (67%; 95%CI: 57.2–75.5), oropharyngeal lesions (7.0%; 95%CI: 3.4–14.0), and systemic symptoms (51.1%; 95%CI: 33.8–68.1). The average duration of fever was 8 days and the average duration of rash was 12 days.

The rate of hospitalization was 21.2% (95%CI: 10–39.5) while the rate of human monkeypox patients with good clinical outcomes was 96.2% (95%CI: 83.1–99.3) and 15% (95%CI: 9.4–23.0) had severe illness. The average length of hospitalization was 25 days and the mortality rate was 5.6% (95%CI: 2.7–11.3). All patients had detectable viral DNA in their upper respiratory tract swabs, skin, genital and anal lesions, 57.1% in urine, and 85.7% in blood. Among human monkeypox referred to sexual health clinics, the prevalence of anogenital lesions was 93.8% (95%CI: 87.2–97.1), and polymorphous rash skin lesions was 49.3% (95%CI: 39.7–58.9). Regarding laboratory findings, there were raised transaminase levels (50%), low blood urea nitrogen level (61%), hypoalbuminemia (50%), leukocytosis (45%), and thrombocytopenia (35%).

We investigated the clinical features of human monkeypox in this epidemic where there are marked variations in transmission route, mean age, gender distribution, and clinical symptoms compared to previous outbreaks. Being male, MSM, sex without a condom, high-risk behaviors, HIV status, and other concurrent STDs appear to be risk factors for human monkeypox inter-human transmission. Patients visiting sexual health clinics with a vesicular-papular rash after a 3–4 day fever, MSM with inguinal lymphadenopathy, and anogenital ulcers should be

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considered human monkeypox suspects. Further larger studies are urgently needed to confirm the present findings.

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Saeed Sahebi: Writing and Editing the draft. Masoud Keikha: Study design, data collection, Writing and Editing the draft.

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Registration of research studies

1. Name of the registry: Not applicable.
2. Unique Identifying number or registration ID: Not applicable.
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All the authors of this paper accept full responsibility for the work and/or the conduct of the study, had access to the data, and controlled the decision to publish.

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Declaration of competing interest

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Saeed Sahebi
Research Committee, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

Masoud Keikha*
Antimicrobial Resistance Research Center, Mashhad University of Medical Sciences, Mashhad, Iran
Department of Microbiology and Virology, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

* Corresponding author. Department of Microbiology and Virology, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.
E-mail address: keikham971@mums.ac.ir (M. Keikha).