



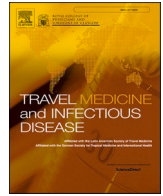
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## A review on insights and lessons from COVID-19 to the prevent of monkeypox pandemic

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### ABSTRACT

Re-emerging of monkeypox virus (MPXV), a neglected viral zoonotic disease, is a potential global threat. In the current COVID-19 pandemic status, the increasing reporting of positive cases of human MPXV in most countries of the world is a major reason for concern. This paper aims to describe the insights and lessons from COVID-19 pandemic in preventing the impending danger MPXV. In order to prevent further outbreak of disease, identify and control of MPXV transmission routes is necessary. Public health authorities should be vigilant and applied of effective strategies to mitigate the potential spread of MPXV. To address research gaps related to MPX outbreaks, national, regional, and international collaborations are required in time. Finally, the lessons and insights put forward point to the fact that, like the COVID-19 pandemic, people's health by and large depends on the decisions of government officials and people must continue to adhere to health principles. Hence, governments and policymakers must take appropriate precautionary measures to prevent similar crises like COVID-19 in the world.

### 1. Introduction

Today, zoonotic viruses are the most serious threat to global health and cause outbreaks of emerging infectious diseases (EIDs) [1]. Human monkeypox (MPX) is one of the zoonotic infections that caused by monkeypox virus (MPXV) which has a large and double-stranded DNA [2]. MPXV is typically a self-limiting disease, that symptoms lasting 2–4 weeks. The mortality rate of MPXV infection is vary considerably ranging between 1 and 11% [3,4]. To date, the majority of reported deaths have involved young children who were not part of the smallpox vaccinated population and people with HIV [4]. Following the eradication of smallpox in the most countries around the globe, the world health assembly declared a moratorium on smallpox vaccination programmes in 1980 [5]. About 40 years after the cessation of vaccination, with the increase in the number of people infected with MPXV, re-emergence of this infection was observed [6]. Hence, MPXV was classified as an emergent disease by the World Health Organization Research and Development (WHO R&D) Blueprint in 2018 [7]. MPXV was rarely seen outside the African continent. It has generally spread beyond the African continent due to the importation of animals and

international travel [5]. As well as, the appearance of cases outside of Africa, emphasizes the disease's potential for geographical spread and global significance [8,9]. While the world has not yet surpassed the COVID-19 pandemic, the increasing reporting of positive cases of human MPXV in the several non-endemic countries is a major reason for concern [10]. The exact way of MPXV transmission to humans is still unknown and there are few genomic studies on the origins of MPXV outbreaks [11,12]. Based on previous studies, nosocomial and household transmission including contact with body fluids, respiratory droplets from infected cases and contaminated aerosols are the major routs of person-to-person transmission of MPXV [13,14]. This virus could potentially remain infectious for long periods of time in the environment [15]. As a lesson from the COVID-19 pandemic and the suffers it has imposed on the world's healthcare systems, it is expected that will be prevented another dangerous pandemic, cleverly [16]. In this study, we describe the insights and lessons from COVID-19 to curb the occurrence of MPXV pandemic and plausible transmission routes.

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## 2. Epidemic scenario of the MPXV

MPXV was first identified in Africa in 1958 especially in rural rain-forest areas of West Africa, the poorest and less privileged country in the world [17]. The first human case of MPXV was discovered in the Democratic Republic of the Congo (DRC) in 1970 [4,18]. Also, the first outbreak of human MPXV was reported in that country in 2003. After that it occurred in South Sudan (2005) and Nigeria (2017) [19,20]. Outside of Africa, MPXV outbreak was reported in the Midwest states of the United States of America in 2003 and then observed in United Kingdom, Israel, and Singapore [19,21]. After a period of relaxation in human MPXV infection, one case was recognized in an individual who travelled to the UK from Nigeria on May 7, 2022. Until August 19, 2022, that the MPXV began to spread around the world, 41358 cases have been confirmed in 94 locations worldwide. Of these, 40971 and 387 confirmed cases were reported in non-endemic and endemic countries, respectively [22]. At the time of writing, 12 deaths have been reported so far, 5 of which occurred in locations that have not historically reported MPXV. The highest number of cases has been reported from the United States of America, Spain, Germany, Brazil, the United Kingdom, France, Canada and Netherlands [22,23]. The size and spread of outbreak clusters across Europe, Americas, the Eastern Mediterranean and Western Pacific regions are growing rapidly. On July 23, 2022, WHO declared the escalating global MPXV outbreak as a Public Health Emergency of International concern due to the rapid increase in cases [23,24].

## 3. Diagnosis

MPXV infection is diagnosed using clinical signs and laboratory tests. The symptoms of MPXV are similar to those of smallpox but less severe [25]. The incubation period for MPX is typically 7–14 days, but it can last up to three weeks [26]. The general symptoms of this disease are fever, severe headache, back pain, severe asthenia, myalgia, and lymphadenopathy [27]. The main difference between MPX and smallpox symptoms is that, unlike smallpox, MPX causes lymphadenopathy [28]. The rash usually appear up to 5 days after the onset of fever and affects the face, palms, soles, oral mucosa, genitals, and conjunctiva [29]. The most definitive and accurate laboratory method for diagnosing MPX is real-time PCR (RT-PCR). The optimal diagnostic specimens for MPX are skin lesions, the roof or fluid from vesicles and pustules, and dry crusts [30]. Antigen and antibody detection methods, such as enzyme-linked immunosorbent assay (ELISA) and immunohistochemistry, do not provide a specific diagnosis for MPX because orthopoxviruses can cross-react serologically [31]. Electron microscopy is ineffective for specific diagnosis because MPX virus is morphologically indistinguishable from other poxviruses, but it does provide evidence that the virus belongs to the *Poxviridae* family [29].

## 4. Treatment

The majority of people infected with MPX heal without medical treatment. Patients with gastrointestinal symptoms such as vomiting and diarrhea require oral/intravenous rehydration to balance gastrointestinal fluids [32]. There are several treatment options for MPX infection, including antiviral drugs, vaccinia immune globulin (VIG), and vaccine. Tecovirimat (ST-246 or TPOXX), the first antiviral for the treatment of smallpox, was approved by the US Food and Drug Administration (FDA) in 2018 [33]. Tecovirimat prevents the formation of enveloped virions and the spread of the virus within an infected host by inhibiting the viral envelope protein P37, a protein that is highly conserved in all orthopoxviruses [34]. Cidofovir (Vistide) and brincidofovir (CMX001 or Tembexa) are viral DNA polymerase inhibitors [35] that have been shown to inhibit MPXV replication *in vitro* and *in vivo* [36]. Cidofovir (injectable) is an acyclic nucleoside phosphate that was approved by the FDA in 1996 for the treatment of cytomegalovirus

(CMV) retinopathy in AIDS patients [37]. Cidofovir has been shown to be effective against poxviruses in preclinical and *in vitro* studies [28]. Brincidofovir (oral) is a liquid conjugate of cidofovir [36] that was approved by the FDA in 2021 for the treatment of smallpox infection and may have less renal toxicity than cidofovir [38]. VIG is a hyperimmune globulin that is used to treat complications associated with vaccinia vaccination [39]. The use of VIG can be considered a potential treatment for orthopoxviruses (including MPX), though there is no data on its efficacy against these viruses [33].

Vaccination is widely accepted as an effective and low-cost method of preventing and even eradicating infectious diseases. Vaccines can provide protection by inducing herd immunity in unvaccinated individuals [40]. There is currently no specific vaccine against MPX infection. Smallpox vaccination has been reported to provide 85% protection against MPXV [41]. ACAM2000 was approved by the FDA in 2007 for use against smallpox. Because ACAM2000 is made from a live, replication-competent Vaccinia virus, it can cause serious side effects in immunocompromised persons [42]. Jynneos (Imvamune or Imvanex) was approved by the FDA in 2019 for the prevention of both MPX and smallpox. Jynneos is a non-replicating modified Vaccinia Ankara virus vaccine that does not produce live viruses in vaccinated individuals, making it a safer choice than ACAM2000 [43].

## 5. Result and discussion

Disaster risk management can be extremely challenging during a pandemic. As a result, it is critical that governments implement special policies and plans for dealing with multiple risks during such times. The ability to successfully manage disasters is proportional to the amount of knowledge gained from the on-going experience (COVID-19 pandemic) [44,45].

MPXV like COVID-19 pandemic is a health, political and socio-economic crisis that will have serious consequences in society if not controlled promptly [46]. Although most countries around the world, are still fighting the COVID-19 pandemic, they should not neglect the risk of MPXV. On a positive note, over the past three years, valuable experiences and lessons have been learned in the fight against the COVID-19 pandemic, which by using them, the re-emerging virus can be easily prevented and controlled [44]. The literature review demonstrate that the causes of MPXV re-emerging especially in endemic regions and developing countries, are including insufficient data about transmission route and potential reservoir hosts, inadequate skills and experiences of health workers, expensive detection methods and lack of public health intervention strategies [47–49]. In this regard, Reynolds et al. (2019) reported that the role of MPXV ecology and transmission route in disease outbreak should be strengthened. They also reported that enhanced research to identify important sources of zoonotic transmission of MPXV can reduce human infections with this pathogen [50]. Beside, Sadeuh-Mba et al. (2019) findings highlighted, local capacity strengthening is needed for early detection and control of MPXV in the affected regions [17]. Adler et al. (2022) study on viral kinetics of MPXV, showed that prolonged upper respiratory tract viral DNA shedding after skin lesion resolution are challenging and prospective studies about antivirals is necessary for controlling the virus [4]. As well as, Verreault et al. (2013) examined the longevity of the MPXV in a laboratory controlled aerosol and suggested that a potential of MPXV to retain infectivity in aerosols is more than 90 h [15]. However, to our knowledge, very few studies have been conducted in this field and aerosols transmission of MPXV is still remain controversially.

It has also been reported that the poxviruses has a very high environmental persistence compared to other enveloped viruses, as fomites may remain infected for months [51,52], but fortunately these viruses are sensitive to common disinfectants (sodium hypochlorite, formaldehyde, sodium hydroxide, peracetic acid, quaternary ammonium compounds) [52,53]. In fact, an integrated active national framework monitoring system can help to control the MPXV epidemic in the future.

In this regard, set up a regional surveillance and monitoring centers is a good option which consequently suspicious patients are quickly identified and save overall costs [54]. Today, globalization, cross-border migration and international trade which interconnected different societies and populations, highlighted the risk of dangerous emerging and re-emerging infectious diseases [55]. Hence, universal health care should be considered as a social norm worldwide. In view of this observation, veterinary and environmental health sectors should be continuously monitoring zoonotic disease and collecting reliable data that can be play a vital in preventing and controlling viral endemics and pandemics. To support rapid response and long-term monitoring of MPXV in the environment, active engagement with environmental health engineering's in the academic communities should be investigated. Multiple presences indicate that MPXV has become a significant travel-related disease, and health professionals must remain alert in fighting the virus transmission.

## 6. Recommendations

- Proper and principled information about the risks of MPXV and provision of preventive recommendations by health authorities in the community.
- Continuing to limit public gatherings, observe safe distance, urgent remodeling of the healthcare sector in all nations.
- Continuous monitoring of international travelers that have symptoms of MPXV, especially with fever and rash by health-care workers around the world.
- Update of detection methods of MPXV, prepare adequate personal protective equipment (PPE, gloves, water-resistant gown, FFP2 respirator) for health professionals especially in poor communities.
- Allocating sufficient funds to identify the transmission pattern of the disease, zoonotic hosts, reservoirs and vectors of the MPXV.
- Understanding of the ecological, social and scientific interconnections between endemic and non-endemic areas for ending chains of MPXV transmission.
- Use of 0.1% sodium hypochlorite (dilution 1:50) for disinfection of contaminated surfaces, washing of clothing and linens at 60 °C.
- The dissemination of dust and aerosols should be reduced during routine cleaning in healthcare settings.
- Use of the smallpox vaccine for preventing MPXV transmission according to the Centers for Disease Control (CDC) recommend.
- Special attention to potential impact of psychological challenges in society and mental support of patients during epidemics.

## 7. Conclusion

Because of the overlap of MPXV with the present pandemic, the world is in a more challenging situation and people will face more severe economic, health and social upheavals, as in the last three years. Immediate spread of MPXV to other countries is a global health security issue, and implementation of public health measures by policymakers is emergency. In light of the current situation, the importance of human MPXV to public health, should not be underestimated. Our findings highlight the need to strengthen regional capacity for early detection, prevention, management and then control of MPXV in world. At the moment, all efforts should be focused to prevent the entering of MPXV to healthcare facilities which are still grapple with the challenges imposed by the current pandemic. In this regard, International support for increasing monitoring capabilities and early detection of MPXV cases are essential tools for understanding the epidemiology of the re-emerging infectious disease. Furthermore, a better understanding of the MPXV transmission pathways is required so that public health officials can develop and implement intervention strategies to reduce the risk of human infection.

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## Author's contributions

**Sara Hemati:** Conceptualization, Methodology, Investigation, Validation, Formal analysis and Writing - Review Original Draft. **Marzieh Farhadkhani:** Methodology, Investigation, Writing - Original Draft and editing. **Samira Sanami:** Methodology, Investigation and Writing - Original Draft. **Fazel Mohammadi-Moghadam:** Conceptualization, Methodology, Writing - Review & Editing, Visualization and Supervision.

## Declaration of competing interest

All Authors have declared no conflict of interest.

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