

Differences in the US Mpox Outbreaks of 2003 and 2022: A Review

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Abstract

Objectives: This research aims to focus on the differences in mpox outbreaks that occurred in 2003 and 2022 in the United States. **Methods:** We searched the following databases Medline, Google Scholar, Gayle Power Search, PubMed, and Springerlink using the following search terms “mpox virus”, “MPX”, “mpox in the US”, “US mpox virus 2003”, “US mpox virus 2022”, “US mpox outbreak 2003” and US mpox outbreak 2022”. The only articles selected were those written between 2003 and 2022. **Results:** Findings showed more Mpox research was conducted during the first US Mpox outbreak in 2003 compared to the US Mpox outbreak in 2022. Findings also indicated that the mpox outbreak of 2003 consisted of more animal-to-human transmissions acquired from sick prairie dogs compared to more human-to-human from an infected international traveler from Nigeria to the US. **Conclusion:** Major differences in the mpox outbreaks in the US include the number, location of lesions, and transmission type. We recommend further research to increase awareness of the human-to-human transmission of mpox via sexual contact to assist healthcare professionals and public health leaders in providing prevention and wellness in US communities.

Keywords

Mpox, Mpox Virus, Mpox Outbreak, US Mpox 2003, US Mpox 2022

1. Introduction

The Mpox virus (MPXV) is a poxvirus disease of the Genus *Orthopoxvirus* that can produce disease in animals and Humans [1]. Monkeys housed in a Denmark research lab during the late 1950s became infected with a pox-type illness while engaged in poliovirus vaccine research [2]. More than a decade later in 1970, it was noted that the first animal-to-human case occurred in the Democratic Republic of Congo (DRC) in a child less than one year of age [2]. Since the first

presentation of the pox-like illness occurred in monkeys, the virus was named “mpox” [3]. Recent literature indicates mpox is prevalent in Central and Western Africa and the reservoir of the mpox virus remains unknown [4]. The mpox virus stems from the West African clade and the Congo Basin African clade [4]. The West African clade consists of mpox virus cultures isolated from infected individuals from Nigeria, and Liberia along with ones spread from Ghana to the United States [5]. In contrast, the Congo Basin African clade consists of mpox virus cultures isolated from individuals in Cameroon, the Republic of the Congo, Gabon, and the DRC [5]. Research indicates that the West African clade mpox is milder than the DRC clade and is responsible for the mpox outbreak in the US [6].

Rope squirrels, tree squirrels, Gambian pouched rats, and dormice are noted to be hosts for the double-stranded DNA mpox virus according to researchers [7]. Transmission during the 2003 outbreak transpired by contact with animal body fluids, bites, or lesions compared to transmission by intimate skin-to-skin contact with human body fluids, and lesions [8].

2. Methods

Data Collection

The following databases were searched: Medline, Google Scholar, Gayle Power Search, PubMed, and SpringerLink using the following search terms “mpox virus”, “MPX”, “mpox in the US”, “mpox virus 2003” and “mpox virus 2022”. Information extracted from each article included author name, publication title, publication year, publication type, clade, transmission type, and lesion location. Additionally, we obtained information from the websites of leading health experts such as the Centers for Disease Control and Prevention and the World Health Organization.

Following the identification of every article collected from the five databases, we removed duplicates and all articles about mpox outbreaks in other countries and animal studies to focus only on articles referring to the mpox outbreak in the US among human subjects. Other exclusions included articles that focused on smallpox and data unrelated to the topics of interest. Only articles written between 2003 and 2022 were selected. Article types appropriate for extraction consisted of research articles, non-research articles, case reports, review articles, reports, opinions, views, perspective articles, editorials, letters to the editor, and commentaries.

3. Results

The thorough review of literature collected from PubMed, Medline, Google Scholar, Springerlink, and Gayle Power Search, resulted in 54 out of 69 articles, respectively. This review includes 4 opinion, view, and perspective articles, 6 case reports, 6 three letters to the editor, 1 editorial, 6 commentaries, 7 reports, 13 research, 7 review articles, and 4 non-research articles (See

Figure 1 below).

As suspected, more mpox research was conducted during the 2003 outbreak compared to the amount of research conducted for the 2022 mpox outbreak in the US. Article types published during the 2003 mpox outbreak consisted of research and review articles whereas during the 2022 mpox outbreak, most of the information came from reports, commentaries, opinions, viewpoints, and perspective articles and letters to the editor. The 2022 mpox has disseminated very little research literature compared to 2003 (see Table 1).

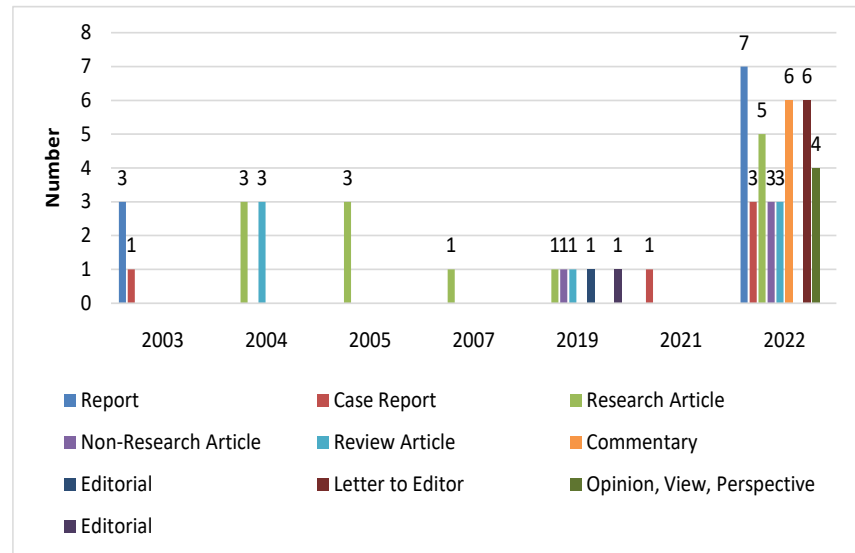


Figure 1. Number of US mpox peer reviewed articles from 2003-2022.

Table 1. US Mpox outbreak 2003 and 2022 articles.

Author	Year	Article Title	Article Type
Huhn <i>et al.</i>	2005	Clinical characteristics of human mpox, and risk factors for severe disease	Research
Guarner <i>et al.</i>	2004	Mpox transmission and pathogenesis in prairie dogs	Research
Sejvar <i>et al.</i>	2004	Human mpox infection: A family cluster in the midwestern United States	Research
Bayer-Garner	2005	Mpox virus: Histologic, immunohistochemical and electron-microscopic findings	Research
Likos <i>et al.</i>	2005	A tale of two clades: Mpox viruses	Research
Reynolds <i>et al.</i>	2007	Spectrum of infection and risk factors for human mpox, United States, 2003	Research
Beer & Rao	2019	A systematic review of the epidemiology of human mpox outbreaks and implications for outbreak strategy	Research
Bunge <i>et al.</i>	2022	The changing epidemiology of human mpox—A potential threat? A Systematic Review	Research
Benites-Zapata <i>et al.</i>	2022	Clinical features, hospitalization and deaths associated with mpox: A systematic review and meta-analysis	Research
Bragazzi <i>et al.</i>	2022	Epidemiological trends and clinical features of the ongoing mpox epidemic: A preliminary pooled data analysis and literature review	Research

Continued

Jamali <i>et al.</i>	2022	Human mpox outbreaks from 2001 to 2021—A systematic review	Research
Thornhill <i>et al.</i>	2022	Mpox virus infection in humans across 16 countries—April-June 2022	Research
Ligon, L.	2019	Mpox: A review of the history and emergence in the Western hemisphere	Review
Di Giulio & Eckburg	2004	Human mpox: An emerging zoonosis	Review
Alah <i>et al.</i>	2004	The story behind the first few cases of mpox infection in non-endemic countries, 2022	Review
Reed <i>et al.</i>	2004	The detection of mpox in humans in the western hemisphere	Review
Kmiec & Kirchhoff	2022	Mpox: A New Threat?	Review
Titanji <i>et al.</i>	2022	Mpox: A contemporary review for healthcare professionals	Review
Al-Gburi & Namuq	2022	A Review of the Recent Mpox Outbreak in 2022	Review
Centers for Disease Control and Prevention	2003	Update: Multistate outbreak of mpox—Illinois, Indiana, Kansas, Missouri, Ohio, and Wisconsin, June 20, 2003	Report
Centers for Disease Control and Prevention	2003	Update: Multistate outbreak of mpox—Illinois, Indiana, Kansas, Missouri, Ohio, and Wisconsin, June 27, 2003	Report
Centers for Disease Control and Prevention	2003	Update: Multistate outbreak of mpox—Illinois, Indiana, Kansas, Missouri, Ohio, and Wisconsin, July 11, 2003	Report
Aden <i>et al.</i>	2022	Rapid diagnostic testing for response to the mpox outbreak—laboratory response network, United States, May 17-June 30, 2022	Report
Charniga <i>et al.</i>	2022	Estimating the incubation period of mpox virus during the 2022 multi-national outbreak	Report
Minhaj <i>et al.</i>	2022	Mpox Outbreak—Nine States, May 2022	Report
Payne <i>et al.</i>	2022	Incidence of mpox among unvaccinated persons compared with persons receiving ≥ 1 Jynneos vaccine dose—32 U.S. Jurisdictions, July 31-September 3, 2022	Report
Philpott <i>et al.</i>	2022	Epidemiologic and Clinical Characteristics of Mpox Cases—United States, May 17-July 22, 2022	Report
Rao <i>et al.</i>	2022	Mpox in a traveler returning from Nigeria—Dallas, Texas, July 2021	Report
Bosworth <i>et al.</i>	2022	Mpox: An old foe, with new challenges	Commentary
Yang, Z.	2022	Mpox: A potential global threat?	Commentary
Laurence	2022	The recent rise in sexually transmitted infections in the United States was a harbinger of the new mpox pandemic	Commentary
McAndrews <i>et al.</i>	2022	Early human judgment forecasts of human mpox, May 2022	Commentary
Ennab <i>et al.</i>	2022	Rise of mpox: Lessons from COVID-19 pandemic to mitigate global health crises	Commentary
Taseen <i>et al.</i>	2022	Post-pandemic world at the mercy of mpox virus outbreak: Time to worry or not?	Commentary
Daskalakis <i>et al.</i>	2022	Mpox: Avoiding the mistakes of past infectious disease epidemics	Opinion, View, Perspective
Stephenson	2003	Mpox outbreak a reminder of emerging infections vulnerabilities	Opinion, View, Perspective
Rio	2022	Update on the Mpox Outbreak	Opinion, View, Perspective

Continued

Velavan & Meyer	2022	Mpox 2022 outbreak: An update	Opinion, View, Perspective
Petersen <i>et al.</i>	2019	Human mpox—Epidemiologic and clinical characteristics, diagnosis, and prevention	Non-research
Kumar <i>et al.</i>	2022	The 2022 outbreak and the pathobiology of the mpox virus	Non-research
Costello <i>et al.</i>	2022	Imported Mpox from Internal Traveler, Maryland, USA, 2021	Non-research
Bhattacharya <i>et al.</i>	2022	Recently spreading human mpox virus infection and its transmission during COVID-19 pandemic period: A travelers' prospective	Non-research
Awan <i>et al.</i>	2022	Mpox: A new threat at our doorstep!	Letter to Editor
Costello <i>et al.</i>	2022	Imported Mpox from Internal Traveler, Maryland, USA, 2021(Response)	Letter to Editor
Heskin <i>et al.</i>	2022	Transmission of mpox virus through sexual contact—A novel route of infection	Letter to Editor
Minhaj <i>et al.</i>	2022	Imported mpox from international traveler, Maryland, USA, 2021	Letter to Editor
Thakur <i>et al.</i>	2022	Mpox virus (MPX) in humans a concern: Trespassing the global boundaries	Letter to Editor
Worsley <i>et al.</i>	2022	Decline in antibody responses to SARS-CoV-2 post-vaccination poses a risk to health care workers	Letter to Editor
Anderson <i>et al.</i>	2003	A case of severe mpox virus disease in an American child: Emerging infections and changing professional values	Case Report
Basgoz <i>et al.</i>	2022	Case 24-2022: A 31-year-old man with perianal and penile ulcers, rectal pain, and rash	Case Report
Edmiston <i>et al.</i>	2003	The mpox virus outbreak: Reflections from the frontlines	Case Report
Costello <i>et al.</i>	2021	Imported mpox from international traveler, Maryland, USA, 2021	Case Report
Ajmera <i>et al.</i>	2022	Mpox—An emerging pandemic	Case Report
Ortiz-Martinez <i>et al.</i>	2022	Mpox—a description of the clinical progression of skin lesions: A case report from Colorado, USA	Case Report

4. The U.S. Mpox Outbreak, 2003

The mpox virus initially surfaced in 1958 by way of animal-to-animal transmission and resurfaced in the Democratic Republic of Congo (DRC) via animal-to-human transmission in 1970 [9]. Studies show that the occurrence of human-to-human transmission was endemic to only DRC [10]. The mpox virus of 2003 consisted of no human-to-human infections, and only animal-to-human transmissions were reported at that time [10] [11] [12]. Before 2003, the mpox virus did not reach the United States until after a sick prairie dog from Ghana infected a small child in the Midwest [13]. Exotic animals such as prairie dogs, tree squirrels, rope squirrels, dormice, Gambian giant pouched rats, brush-tailed porcupines, and striped mice from Africa were being transported to the US and sold as pets [13]. More specifically, the parents of a small child purchased a prairie dog from a flea market, and shortly after being in the home; the dog became sick and died [13]. The child in turn developed a rash covering her face, chest upper, and lower extremities, and bottom of her feet along with swollen

lymph nodes, and problems swallowing and breathing [13]. Another animal-to-human transmission during the 2003 mpox outbreak involved a Milwaukee, Wisconsin veterinarian who presented to the emergency room complaining of swollen lymph nodes and a skin lesion after exposure to a sick prairie dog [14]. Lesions associated with the 2003 US mpox outbreak tended to start in the face followed by the arms/hands, legs/feet, head/neck, chest/abdomen, back, palms, groin/buttocks, soles, and mucosa [15]. Another characteristic of the lesions associated with the 2003 mpox outbreak involved determining the “rash burden” developed by the World Health Organization [15]. A “moderate” rash consisted of 26 - 100, a “grave” rash consisted of 101 - 250 lesions and a “plus grave” rash consisted of greater than 250 lesions [15] (See **Table 2**).

Table 2. 2003 US mpox outbreak.

Year	Author(s)	Title	Clade	Transmission	Lesions
2003	Anderson <i>et al.</i>	A case of severe mpox virus disease in an American child: Emerging infections and changing professional values	West African	Animal-human	Face, mouth, chest, trunk, palms, soles
2003	Centers for Disease Control and Prevention	Update: Multistate outbreak of mpox—Illinois, Indiana, Kansas, Missouri, Ohio, and Wisconsin, 2003	West African	Animal-human	Lesions in the oropharynx, skin rash lesions
2004	Di Giulio & Eckburg	Human mpox: An emerging zoonosis	West African	Animal-human	Generalized, palms, soles
2004	Ligon, L.	Mpox: A review of the history and emergence in the Western hemisphere	West African	Animal-human	Face, head, trunk & extremities
2004	Reed <i>et al.</i>	The detection of Mpox in humans in the Western Hemisphere	West African	Animal-human	Face, scalp, hands, arms, legs, trunk, perineum, conjunctivae, buccal mucosa
2004	Sejvar <i>et al.</i>	Human Mpox infection: A family cluster in the Midwestern US	West African	Animal-human	Face, trunk, palms, soles
2005	Bayer-Garner	Mpox virus: Histologic immunohistochemical and electron-microscopic findings	West African	Animal-human	Generalized, soles, palms
2005	Huhn <i>et al.</i>	Clinical characteristics of human Mpox, and risk factors for severe disease	West African	Animal-human	Generalized, soles, palms
2005	Likos, <i>et al.</i>	A tale of two clades: Mpox viruses	West African	Animal-human	Febrile rash
2019	Petersen <i>et al.</i>	Human mpox—Epidemiologic and clinical characteristics, diagnosis, and prevention	West African	Animal-human	Face, across the body, hands, legs, feet
2022	Bunge <i>et al.</i>	The changing epidemiology of human mpox—A potential threat? A systematic review	West African	Animal-human	Face, palms, soles
2022	Benites-Zapata <i>et al.</i>	Clinical features, hospitalization and deaths associated with mpox: A systematic review and meta-analysis	West African	Animal-human	Head, neck, hands, palms, arms,

5. The U.S. Mpox Outbreak, 2022

There had not been any mpox globally since the 2003 outbreak until it resurfaced in the United Kingdom in 2022 [16]. Literature indicates that a British traveler contracted the virus after returning from Nigeria and through contact tracing, more individuals were identified as having had contact with the same British traveler [16] and that all the individuals were gay or bisexual. In May 2022, a Massachusetts male contracted the mpox virus after engaging in unprotected sexual intercourse with males while in Canada [16]. Another person encountered the same British traveler in Florida where he and his husband engaged in unprotected sexual intercourse with an unknown number of men resulting in the contraction of the mpox virus [17].

In the current mpox outbreak, the virus was primarily contracted by men having unprotected sex with other men, who had the human immunodeficiency virus (HIV), syphilis, and other sexually transmitted diseases [17] [18]. Most all the individuals infected had smaller manifestations of the anogenital lesions in the 2022 outbreak compared to greater than one hundred lesions covering the upper and lower extremities, face, soles of feet, and palms of hands during the 2003 outbreak [19] (See **Table 3**).

6. Discussion

Viral Zoonosis consists of viruses that are transmitted from animals to humans such as Monkeypox, a viral zoonosis that comes from the Orthopoxvirus genus of the Poxviridae group [20]. The Mpox virus erupted initially in the Congo basin of central Africa in the 1970s [20] and presented again in the United Kingdom, Singapore, Israel and again in the United States 2018 to 2022 [20]. Zoonotic transmission, also referred to as animal-to-human transmission results from close contact with blood or body fluids from an infected animal to a human [20]. This review indicates that the first mpox outbreak in the US involved animal-to-human transmission with the suspected host being infected prairie dogs imported from West Africa and the second mpox outbreak involved human-to-human transmission among men having sex with men initiated by an individual that traveled from Nigerian to the US [20]. The literature notes that although the mpox virus is contracted by skin-to-skin contact, there remains no definitive data on the virus being sexually transmitted currently [20]. There are several differences between the two US out-breaks. The first difference involves the number and location of lesions. For example, in 2003, lesions were numerous at greater than 100, starting in the face, covering the whole body, and progressing to the palms of the hands and soles of the feet which are characteristic of mpox [20]. In the current mpox outbreak, the lesions are localized to the mouth, anus, and genitalia and are less numerous, and appear before other symptoms [20]. Another distinguishing characteristic of mpox compared to other “pox-like” disorders is Lymphadenopathy which is uncharacteristic of smallpox and chickenpox [20]. This research aims to focus on the differences in

Table 3. 2022 US mpox outbreak.

Year	Author(s)	Title	Transmission	Clade	Lesions
2021	Costello <i>et al.</i>	Imported Mpox from Internal Traveler, Maryland, USA, 2021	Human-Human	West African	Forehead, nose, mouth, arms, trunk, inner thighs
2022	Basgoz <i>et al.</i>	Case 24-2022: A 31-year-old man with perianal and penile ulcers, rectal pain, and rash	Human-Human	West African	Perianal, penile
2022	Ajmera <i>et al.</i>	Mpox—An emerging pandemic	Human-Human	West African	Mouth, tongue, face
2022	Alah <i>et al.</i>	The story behind the first few cases of mpox infection in nonendemic countries, 2022	Human-Human	West African	Genital areas
2022	Benites-Zapata <i>et al.</i>	Clinical features, hospitalization and deaths associated with mpox: A systematic review and meta-analysis	Human-Human	West African	Pelvic, groin, genitalia
2022	Bhattacharya <i>et al.</i>	Recently spreading human mpox virus infection and its transmission during COVID-19 pandemic period: A travelers' prospective	Human-Human	West African	Not reported
2022	Bosworth <i>et al.</i>	Mpox: An old foe, with new challenges	Human-Human	West African	Not reported
2022	Bragazzi <i>et al.</i>	Epidemiological trends and clinical features of the ongoing mpox epidemic: A preliminary pooled data analysis and literature review	Human-Human	West African	Genital and anal lesions (ulcers and vesicles)
2022	Daskalakis <i>et al.</i>	Mpox: Avoiding the mistakes of past infectious disease epidemics	Human-Human	West African	Genital and anal region
2022	Minhaj <i>et al.</i>	Mpox outbreak—nine states, May 2022	Human-Human	West African	Genital, perianal area
2022	Kmiec & Kirchhoff	Mpox: A new threat?	Human-Human	West African	Genital, perianal area
2022	Laurence	The recent rise in sexually transmitted infections in the United States was a harbinger of the new mpox pandemic	Human-Human	West African	Anogenital
2022	Ortiz-Martinez <i>et al.</i>	Mpox—a description of the clinical progression of skin lesions: a case report from Colorado	Human-Human	West African	Perineal area and genitals
2022	Rao <i>et al.</i>	Mpox in a traveler returning from Nigeria -Dallas, Texas, July 2021	Human-Human	West African	Face
2022	Singhal <i>et al.</i>	Mpox: A review	Human-Human	West African	Face, oral mucous membranes, genitalia, palms, soles
2022	Thakur <i>et al.</i>	Mpox virus (MPX) in humans a concern: Trespassing the global boundaries	Human-Human	West African	
2022	Thornhill <i>et al.</i>	Mpox virus infection in humans across 16 countries—April-June 2022	Human-Human	West African	Anogenital, mucosal
2022	Kumar <i>et al.</i>	The 2022 outbreak and the pathobiology of the mpox virus	Human-Human	West African	

mpox outbreaks that occurred in 2003 and 2022 in the United States. This study also reviewed the number of research papers compared to commentaries, reports, and case reports written about the US mpox outbreak in 2003 and 2022 to gain more insight into these differences and their impact on population health in the US.

7. Limitations

This review has identified limitations beginning with the limited amount of research conducted about the 2022 mpox outbreak in the United States. Therefore, there were not enough research articles to choose for inclusion. Next, several studies were excluded because they consisted of animal research, and genetic research or was conducted outside of the US. The authors underestimated the limitations of Mpox articles and research. Therefore, due to identified gaps in the literature, more research is recommended to further determine the clinical, social, and psychological impact of the mpox virus globally.

8. Conclusions

In this study, we reviewed various types of articles written during both the 2003 and 2022 mpox outbreaks. We compared the two outbreaks and found that more research was conducted during the first US mpox outbreak compared to the current outbreak.

Major differences in the mpox outbreaks include differences in the number and location of lesions and transmission type. More research is recommended to increase awareness of the human-to-human transmission of mpox via sexual contact to assist healthcare professionals and public health leaders in providing prevention and wellness in US communities.

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Credit Authorship Contribution Statement

The manuscript was conceptualized and written by Sandra Henley, and Stephanie Woods-Crawford provided the final review and critique.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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