Human monkeypox outbreak: global prevalence and biological, epidemiological and clinical characteristics – observational analysis between 1970-2022

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Abstract. – OBJECTIVE: The human monkeypox infection has become the prevalent orthopoxviral disease in humans, and has developed challenging and threatening situations worldwide. This study is aimed at exploring the global epidemiological, biological and clinical characteristics of monkeypox from 1970 to July 1, 2022.

MATERIALS AND METHODS: Information about the monkeypox outbreak and its epidemiological and biological characteristics was obtained from the World Health Organization (WHO), Centers for Disease Control and Prevention (CDC) reports, Pub-Med, and Web of Science. Initially, these two leading international health organizations, and 10 documents were identified; after reviewing, we included WHO and CDC, and six documents in the analysis.

RESULTS: Worldwide, from 1970 to July 1, 2022, the total number of confirmed and suspected cases of human monkeypox disease in endemic and non-endemic nations was 46,915. In endemic regions, the number of confirmed cases has been 2,805 and suspected cases have been 38,327, with a total number of 41,132. However, from May 7, 2022, to July 1, 2022, 5,783 monkeypox cases have been found in 52 non-endemic nations in Europe, the UK, the USA, Australia and the Middle East. The majority of cases have been found in the United Kingdom (1,235), Germany (1,054), Spain (800), France (498), United States (459), Portugal (402), Netherlands (288), Canada (287), Italy (192), Belgium (117), Switzerland (91), Israel (42), Ireland (39), Austria (37), Sweden (28), Brazil (21), and Denmark (20). The clinical presentation of monkeypox disease is mild symptoms, including headache, lymphadenopathy, body aches, severe weakness, and acute onset of fever above 38.5°C. A skin rash initiates as macules or papules, progresses to pustules and vesicles, ulcers, and ultimately transitions to crusted scabs. In a short period of about two months, the monkeypox cases swiftly spread in 52 non-endemic countries with an increased percentage worldwide.

CONCLUSIONS: The geographic pattern of monkeypox disease spread is rapidly shifting from endemic to non-endemic regions. It now involves not only Africa but also Europe, the USA, the UK, Australia and the Middle East. The clinical characteristics of monkeypox infection are mostly mild symptoms, including headache, lymphadenopathy, body aches, severe weakness, and acute onset of fever above 38.5 degrees Centigrade. A skin rash originates as macules or papules, progresses to pustules and vesicles, ulcers, and eventually to crusted scabs. The regional and international health establishments must take priority preventive procedures to break the outbreaks of monkeypox disease across the globe. The physicians, healthcare workers, patients, and public education is of utmost importance to eradicate the disease.

Key Words:

Monkeypox, Prevalence, Outbreak, Clinical characteristics.

Introduction

Monkeypox (MPX) is a zoonotic disease and is currently the prevalent orthopoxviral infection in humans. Monkeypox infection (MPXI) is caused by the monkeypox virus (MPXV). The MPXV is an enveloped double-stranded DNA virus belonging to the genus orthopoxviral, subfamily chordopoxvirinae and family poxviridae¹. Monkeypox is in the same virus family as smallpox, although it has a milder impact.

The monkeypox virus is a brick-shaped, moderately large size of about 200-250 nm, enclosed

by a lipoprotein with a linear double-stranded DNA genome^{2,3}. Apart from dependence on host ribosomes for mRNA translation, poxviruses include replication, transcription, assembly, and egress proteins in their genome⁴. In 1958, monkeypox was first identified as a pox-like disease in monkey colonies consequently, the disease acquired the monkeypox name. The first case of "human monkeypox" was reported in 1970 in the Democratic Republic of the Congo. Afterwards, the disease has been identified in other Central and Western African countries¹. Recently, since May 2022, monkeypox cases have been reported in many non-endemic States in Europe, the United Kingdom, the United States, Australia, the Middle East and other countries in the world^{5,6}.

MPXV can transmit through direct or indirect interaction with body fluids, cutaneous, mucosal lesions, or sores of infected individuals, or with materials that contain infected body fluids such as clothing or linens^{7,8}. The World Health Organization has announced plans to rename the disease soon⁹. This decision followed a call by a group of international researchers to use the name hMPXV, to denote a human version of the monkeypox virus. The researchers realized that the human virus is part of a distinct viral clade of MPXV that is transmitted from humans to humans distinct from the two clades that are transmitted from animals to humans⁹.

Recently, monkeypox has become a challenging and threatening situation worldwide, and literature is lacking to highlight the epidemiologic and biological appearances of human monkeypox. This report is aimed at investigating the global prevalence and biological, epidemiological, and clinical characteristics of monkeypox infections from 1970 to July 1, 2022.

Materials and Methods

This study explored the global prevalence and biological, epidemiological, and clinical characteristics of monkeypox viral infections. The required information was gathered from the World Health Organization (WHO)⁵, Centers for Disease Control and Prevention (CDC)^{6,7}, and weekly reports published by CDC. In addition, we also reviewed PubMed¹⁰ and Web of Science¹¹. Initially, two international organizations and 10 documents were identified from these sources. After screening and reviewing the summary, detailed reports and articles, we

selected the two above international leading health organizations and six documents from which we obtained data and findings to include in the analysis. For the biological and clinical characteristics of monkeypox, we reviewed the literature published by or in the databases of the World Health Organization, CDC, PubMed, and Web of Science. The relevant literature was explored through keyword searches, including "monkeypox", "epidemiology", "incidence", "prevalence", "pathophysiological aspects", "clinical characteristics", and "biological characteristics". After the literature had been shortlisted, the appropriate epidemiological, biological, and clinical characteristics and findings were recorded.

Statistical Analysis

In this study, data were documented, verified, and analyzed, and the findings were expressed in numbers and percentages. The percentage change (%) was calculated by taking the difference between the values and then multiplying it by 100. The percentage change shows the trends of cases during the period.

Results

The global epidemiological figures on the prevalence of human monkeypox cases are presented in Tables I-III. Worldwide, the total number of confirmed cases (Table I, Figure 1) and suspected (Table II) cases of human monkeypox from 1970, to July 1, 2022, has been 46,915. The confirmed cases have been 6,113 (Table I), and the suspected cases have been 38,327 (Table II). When genetically and geographically analyzing the confirmed cases, it results that 2,498 are from the Central African Clade, and 307 are from the West African Clade (Table I). Furthermore, 5,783 cases have been recently reported from 52 non-endemic States in Europe, the UK, the USA, Australia, and the Middle East (Table I, III). Among the 38,327 suspected human monkeypox cases, 38,163 are of the Central African Clade and 164 are of the West African Clade" (Table II, Figure 2).

In endemic regions, the human monkey-pox confirmed cases have been 2,805, and the suspected cases have been 38,327, with a total number of 41,132. Currently, from January 1 2022 to July 1, 2022, 5,783 monkeypox cases have been found in 52 non-endemic countries in Europe, the USA, the UK, Australia and in

Table I. Monkeypox confirmed cases of the Central and West African Clade in Endemic and Non-Endemic regions from 1970 to July 1, 2022.

A. Endemic Regions: i: Central African Countries; ii: Western African countries			
The time in years/decades	Central African Clade	West African Clade	Total
1970-1979	38	9	47
1980-1989	355	1	356
1990-1999	520	0	520
2000-2009	92	47	139
2010-2019	85	195	280
2021		34	34
2022 (Jan-June)	1,408	21	1,429
Sub total	2,498	307	2,805
B. Non-endemic Regions: 52 countr	ries in Europe, the UK, USA, Australia	and the Middle East	
Jan 1 to July 1, 2022	5,783	5,783	
Total			8,588

Ref: 5,6,12-17. A: Endemic Regions [i] Central African Countries: Cameroon, Gabon, Central African Republic and Zaire (Democratic Republic of the Congo [ii] Western African countries: Sierra Leone, Nigeria, Ghana, Liberia and Côte d'Ivoire²⁵.

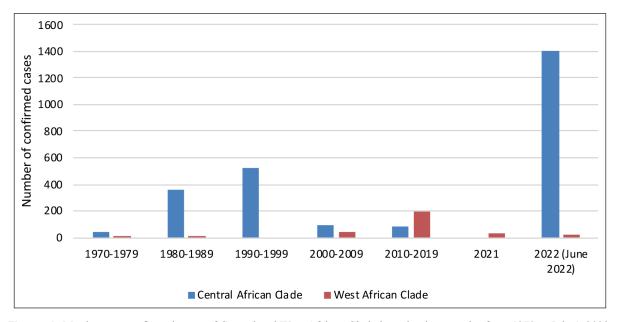


Figure 1. Monkeypox confirmed cases of Central and West African Clade in endemic countries from 1970 to July 1, 2022.

the Middle East (Table III). In the year 2022, the spread of these cases started in early 2022, and subsequent cases until July 1, 2022, were confirmed in 52 non-African/non-endemic countries in Europe, America, Asia, and North Africa, Australia and the Middle East. The majority of these cases are found in non-endemic countries, the United Kingdom (1,235), Germany (1,054), Spain (800), France (498), United

States (459), Portugal (402), Netherlands (288), Canada (287), Italy (192), Belgium (117), Switzerland (91), Israel (42), Ireland (39), Austria (37), Sweden (28), Brazil (21), Denmark (20), Hungry (19), Mexico (15), Norway (15), and remaining countries the cases are less than 15 in each state (Table III, Figure 2). In a short period, the monkeypox cases were swiftly spread in 52 non-endemic countries (Table III).

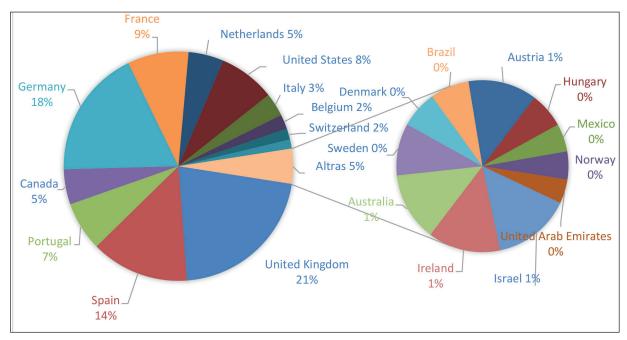


Figure 2. Monkeypox cases in non-endemic regions in Europe, the UK, USA, Australia and the Middle East from January 1 to July 1, 2022.

The clinical characteristics of monkeypox disease classically consist of mild symptoms. The affected individuals by this infection complain of headache, lymphadenopathy, body aches, severe weakness, and acute onset of fever above 38.5 degrees Centigrade. A skin rash originates as "macules or papules and progresses to pustules and umbilicated vesicles, ulcers, and ultimately transitions to crusted scabs" (Table IV).

Discussion

The first case of human monkeypox was found in 1970 in the Democratic Republic of the Congo. Afterwards, the cases have been reported in other central and western African nations^{1,16,17}. The topographical dispersal of human monkeypox virus infection has been speedily shifting from endemic regions to non-endemic regions. The transmission is "animal to human", and "human to human"^{7,8}. The monkeypox virus circulates among some mammals, although there is no specific known reservoir. The literature describes the virus reservoir as tree squirrels in tropical rain forests. Humans can be infected by hunting, killing and skinning these animals¹⁸.

MPXV can spread from animal to person or person to person, once an individual has close contact with the virus from an infected animal, person, or virus-contaminated materials^{19,20}. The virus may also transmit through contact with

Table II. Monkeypox suspected cases of the Central and West African Clade in Endemic regions from 1970 to July 1, 2022.

The period in years/decades	Central African Clade	West African Clade	Total
2000-2009	10,027		10,027
2010-2019	18,788		18,788
2020	6,257		6,257
2021	3,091	98	3,189
2022 (Jan-June)		66	66
Total	38,163	164	38,327

Ref: 5,6,12-17. A: Endemic Regions [i] Central African Countries: Cameroon, Gabon, Central African Republic and Zaire (Democratic Republic of the Congo [ii] Western African countries: Sierra Leone, Nigeria, Ghana, Liberia and Côte d'Ivoire²⁵.

Table III. Monkeypox confirmed cases in Non-Endemic Countries in Europe, UK, USA, Australia, Asia,

Country	June 3, 2022 (n=29). Total Cases: 1,088	June 13, 2022 (n=35). Total cases: 1,678	July 1, 2022 n=52). Total Cases: 5,783	Percentage (%) (Mean values)
1. United Kingdom	302 (27.75%)	470 (28.00%)	1235 (21.35%)	25.70%
2. Germany	80 (7.35%)	189 (11.26%)	1054 (18.22%)	12.27 %
3. Spain	198 (18.19)	275 (16.38%)	800 (13.83%)	16.13 %
4. France	66 (6.06%)	91 (5.42%)	498 (8.61%)	6.69 %
5. United States	34 (3.12%)	64 (3.81%)	459 (7.93%)	4.95 %
6. Portugal	166 (15.25%)	209 (12.45%)	402 (6.95%)	11.55 %
7. Netherlands	54 (4.96%)	60 (3.57%)	288 (4.98%)	4.50 %
8. Canada	80 (7.35%)	123 (7.33%)	287 (4.96%)	6.54 %
9. Italy	20 (1.83%)	50 (2.97%)	192 (3.32%)	2.70 %
10. Belgium	17 (1.56%)	34 (2.20%)	117 (2.02%)	1.92 %
11. Switzerland	10 (0.91%)	19 (1.13%)	91 (1.57%)	1.20 %
12. Israel	2 (0.18%)	4 (0.23%)	42 (0.72%)	0.37 %
13. Ireland	7 (0.64%)	15 (0.89%)	39 (0.67%)	0.73 %
14. Austria	1 (0.09%)	4 (0.23%)	37 (0.63%)	0.31 %
15. Sweden	5 (0.45%)	6 (0.35%)	28 (0.48%)	0.42 %
16. Brazil	0 (0.00%)	3 (0.17%)	21 (0.36%)	0.26 %
17. Denmark	3 (0.27%)	4 (0.23%)	20 (0.34%)	0.28 %
18. Hungary	1 (0.09%)	1 (0.05%)	19 (0.32%)	0.15%
19. Mexico	1 (0.09%)	2 (0.11%)	15 (0.25%)	0.15%
20. Norway	1 (0.09%)	2 (0.11%)	15 (0.25%)	0.15%
21. United Arab Emirates	13 (1.19%)	13 (0.77%)	13 (0.22%)	0.72%
22. Australia	6 (0.55%)	8 (0.47%)	12 (0.20%)	0.40%
23. Romania	0 (0.00%)	0 (0.00%)	11 (0.19%)	0.40%
24. Poland	0 (0.00%)	1 (0.05%)	10 (0.17%)	0.06%
25. Slovenia	6 (0.55%)	7 (0.41%)	9 (0.15%)	0.07%
26. Czechia	6 (0.55%)	6 (0.35%)	8 (0.13%)	0.34%
27. Argentina	2 (0.18%)	3 (0.35%)	6 (0.10%)	0.21%
28. Chile	0 (0.00%)	0 (0.00%)	6 (0.10%)	0.03%
29. Malta	1 (0.09%)	1 (0.05%)	6 (0.01%)	0.05%
30. Iceland	0 (0.00%)	3 (0.35%)	4 (0.08%)	0.14%
31. Finland	2 (0.18%)	3 (0.35%)	4 (0.08%)	0.14%
32. Greece	0 (0.00%)	2 (0.11%)	3 (0.05%)	0.05%
33. Luxembourg	0 (0.00%)	1 (0.05%)	3 (0.05%)	0.03%
34. Peru	0 (0.00%)	(0.00%)	3 (0.05%)	0.01%
35. Benin	0 (0.00%)	(0.00%)	3 (0.05%)	0.01%
36. Bulgaria	0 (0.00%)	(0.00%)	3 (0.05%)	0.01%
37. Colombia	0 (0.00%)	(0.00%)	3 (0.03%)	0.01%
38. Latvia	2 (0.18%)	2 (0.11%)	2 (0.03%)	0.10%
39. South Africa	0 (0.00%)	0 (0.00%)	2 (0.03%)	0.01%
40. Morocco	1 (0.09%)	1 (0.05%)	1 (0.017%)	0.05%
41. Gibraltar	1 (0.09%)	1 (0.05%)	1 (0.017%)	0.05%

Table III (Continued). Monkeypox confirmed cases in Non-Endemic Countries in Europe, UK, USA, Australia, Asia, and
the Middle East from Jan 1 to July 1, 2022. [Ref [§]].

Country	June 3, 2022 (n=29). Total Cases: 1,088	June 13, 2022 (n=35). Total cases: 1,678	July 1, 2022 n=52). Total Cases: 5,783	Percentage (%) (Mean values)
42. Venezuela	0 (0.00%)	1 (0.05%)	1 (0.017%)	0.05%
43. Serbia	0 (0.00%)	0 (0.00%)	1 (0.017%)	0.005%
44. Singapore	0 (0.00%)	0 (0.00%)	1 (0.017%)	0.005%
45. Lebanon	0 (0.00%)	0 (0.00%)	1 (0.017%)	0.005%
46. Georgia	0 (0.00%)	0 (0.00%)	1 (0.017%)	0.005%
47. Taiwan	0 (0.00%)	0 (0.00%)	1 (0.017%)	0.005%
48. Turkey	0 (0.00%)	0 (0.00%)	1 (0.017%)	0.005%
49. South Korea	0 (0.00%)	0 (0.00%)	1 (0.017%)	0.005%
50. Bahamas	0 (0.00%)	0 (0.00%)	1 (0.017%)	0.005%
51. Croatia	0 (0.00%)	0 (0.00%)	1 (0.017%)	0.005%
52. Estonia	0 (0.00%)	0 (0.00%)	1 (0.017%)	0.005%
Total cases	1,088	1,678	5,783	

Ref⁶; n= number of countries. Based on the data recorded on different dates, the percentage change for each country and average percentage were calculated.

body fluids, cutaneous, mucosal lesions, or sores on an infected person or with materials that have touched body fluids or sores, such as clothing or linens". It is also spread by oral, and nasal secretions, and during skin-to-skin contact, such as handshakes, hugging, kissing, and sexual contact. The virus can also cross the placenta from the mother to her fetus⁷. Moreover, close contact during sexual activity can be a rapid source of transmission¹⁹.

The virus enters the body, replicates at the site and spreads to local lymph nodes, and other organs. The incubation period of monkeypox is usually 6 to 13 days, but may range from 5 to 21 days. The primary clinical manifestations of monkeypox diseases are headache, body ache, muscle ache, acute onset of fever, and generalized myalgia^{5,21}. The clinical symptoms start with a secondary viremia leading to 1 to 2 days of prodromal clinical features, such as fever and lymphadenopathy, before the lesions appear on the body. The rash starts in the oro-pharynx and then appears in other parts of the body²². A person is considered to be no longer contagious once the skin lesions have disappeared and a new layer of skin has formed^{5,21}.

The skin lesions begin as macules or papules, which progress to pustules and umbilicated vesicles and ulcers and eventually to crusted scabs²³. The lesions can classically explode and recede in harmony in an anatomical area, unlike vari-

cella. The condition may establish a differential diagnosis including syphilis, chancroid, varicella zoster, herpes simplex, hand-foot-and-mouth disease, and molluscum contagious. Patients are infectious from the onset of symptoms until all scabs have been resolved²⁴. The clinical characteristics of monkeypox cases may be variable. In many cases, patients do not present with the usual clinical symptoms and signs. The common presenting symptoms include fever, oral sores, swollen lymph nodes, and pain when swallowing. The appearance and distribution of the skin rash with vesicular, pustular or ulcerated lesions sometimes begin locally without necessarily spreading diffusely to other parts of the body. The early presentation of a genital or peri-anal rash suggests close physical contact during sexual activities. It has also been reported that in some patients, pustules may appear before other manifestations of the disease, such as fever and lesions at different stages of development⁵.

The monkeypox disease has been debated under geographical and genetic clades. A viral clade is a group of similar viruses based on their genetic sequences and geographical distribution. There are two different genetic clades of the monkeypox virus: the Central African clade (also known as the "Congo Basin" clade), and the West African Clade. The geographical distribution of the Central African clade includes Cameroon, Gabon, the Central African Republic and Zaire (Democratic

Republic of the Congo (DRC). However, the West African clade is linked to the cases reported from Nigeria, Ghana, Liberia, Côte d'Ivoire, and Sierra Leone²⁵. The Central African clade is highly transmissible, and causes a more severe and deadly disease⁵, with a fatality rate of about 11%, while the West African clade has a better prognosis with less than 1% of fatality rate¹⁵.

The outbreak is spreading day by day in non-endemic geographical regions across Europe, the United Kingdom, North America, and Asia. From Jan 1, 2022, to July 1, 2022, there have been 5,783 monkeypox cases in these non-endemic countries. These cases are rapidly increasing in these non-endemic nations and developed threatening situations. The world has already been facing the COVID-19

pandemic's burden and cannot afford the human monkeypox infection to become another one.

Study Strengths and Limitations

This study adds to the literature that has investigated the global prevalence and biological, epidemiological, and clinical characteristics of the human monkeypox virus and its disease. The epidemiological data are based on the prolonged period from 1970 to July 1, 2022. This is not an easy task to obtain the data, especially at a global level. This work attempts to harmonize the information across the countries and provide a piece of additional information to highlight the epidemiological, biological understanding, and transmission dynamics of the monkeypox outbreak. However,

Table IV. Biological and clinical characteristics of Monkeypox virus and disease.

Biological and clinical Characteristics			
Country of origin	The Democratic Republic of the Congo		
Found in monkeys	First time found in monkeys in 1958		
Found in humans	First time found in humans in September 1970		
Characteristics	Size is about 200-250 nm large, brick-shaped, covered by a lipoprotein envelope with a double-stranded DNA genome		
Genetic clades	The "Central African clade (Congo Basin clade), and the West African Clade".		
Geographical distribution of West African clade	Geographically, the WA clade corresponds to the cases reported from Nigeria, Ghana, Liberia, Cote d'Ivoire, and Sierra Leone.		
Geographical distribution of Central African clade	CA Clade includes all isolates from DRC, Republic of the Congo, Cameroon, and Gabon		
Fatality	Central African clade 11% in unvaccinated children. West African clade below 1%		
Spread	Animal to an animal, animal to human, and human to human		
Incubation period	Ranges 5-21 days.		
Seasonal occurrence	Rainy seasons		
Age of affected population	Mainly children and young individuals		
Clinical Characteristics (General)			
Headache	+		
Body ache	+		
Acute onset of Fever	++		
Generalized myalgia	++		
Malaise	+		
Skin Lesions			
Macules	++		
Papules	++		
Pustules	++		
Ulcers	++		
Crusted scabs	++		

Note: +Mild; ++Moderate; +++Severe. Ref^{2-7,12,20,25}.

a limitation of this study is that there is a chance of some missing information as epidemiological data and findings are based on over five decades. The second limitation is that PubMed and Web of Science-based literature is limited, and consists of mainly brief communications and editorials, which are not currently able to support more detailed analyses and conclusions.

Conclusions

Worldwide, from 1970 to July 1, 2022, the total number of confirmed and suspected cases of human monkeypox disease in endemic and non-endemic countries was 46,915. The geographical distribution of the human monkeypox disease is speedily shifting from traditional endemic to non-endemic regions. The monkeypox cases (5,783) have been found in 52 non-endemic countries in Europe, the USA, the UK, Australia and the Middle East. Presently, the majority of these cases are found in the United Kingdom, Germany, Spain, France, United States, Portugal, the Netherlands, Canada, Italy, Belgium, Switzerland, Israel, Ireland, Austria, Sweden, Brazil and Denmark. The clinical presentation of the disease is mainly mild symptoms. The associated complaints include headache, body ache, generalized myalgia, malaise, acute onset of fever and skin lesions. The skin lesions start as macules or papules, progress to pustules, vesicles, and ulcers, and are eventually changed into crusted scabs. The monkeypox virus is a dangerous and contagious disease. To eradicate the disease burden internationally, global health authorities must take priority-based preventive measures to break the outbreaks of monkeypox disease across the globe. The education of physicians, the public, patients, and healthcare workers is of the utmost importance to eradicate this disease.

Conflicts of Interest

The authors declare no conflicts of interest.

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Authors' Contributions

SAM: study concept, data collection, literature review, analysis, writing and editing; DCK: literature review, data checking, writing and editing.

Ethical Statement

In this study, information on the monkeypox outbreak was recorded from publicly available data hence ethical approval was not required.

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