Review Article

Monkeypox Outbreak, a recurring entity that may threaten human existence in the 21st century; a systematic review

ABSTRACT

Background

The resurgence and geographical spread of monkeypox is a public health concern. It is also an implication of weak response and mitigation strategies to disease outbreaks, especially in the endemic regions where there have been sporadic disease outbreaks since five decades ago. This paper aims to review the outbreaks of monkeypox with regards to cases, fatalities, and spread.

Methods: A literature search was conducted in Pubmed using Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, and grey literature was also searched in google scholar. 43 literature (34 peer review articles and 9 grey literature) were included in the review.

Results: 10,970 suspected cases of human monkeypox have been reported across 26 countries since from 1970 to May 2022. One thousand eight hundred twenty-four (1824) cases were confirmed, while 146 deaths have been recorded. The highest outbreaks occurred in the Democratic Republic of Congo(D.R.C.) (14) and the Central African Republic (C.A.R.) (10). The highest mortalities wererecorded from D.R.C. (127) and Nigeria (8).

Conclusion: the spread of monkeypox from one country to 26 countries over a

period of about 5 decades is a threat to human existence if measures are not taken to contain the spread. This study recommends the need to strengthen and increase support for the Surveillance and Detection of monkeypox cases for appropriate management is recommended, especially in resource-limited endemic regions

Keywords: Monkeypox, disease outbreak, threat, human existence, 21st Century

1. INTRODUCTION

There have been several monkeypox outbreaks since the first reported outbreak in 1970 in the Democratic Republic of Congo (DRC), formerly Zaire, these repeated outbreaks calls for public health concern [1]. The cause of monkeypox disease is the monkeypox virus, a rare viral disease, and a member of the orthopoxvirus group of viruses [2]. The disease could be contacted through animal (squirrels and monkeys) bite or direct contact with the animal's lesions or body fluids (zoonotic transmission) [2]. Human-to human transmission most likely through respiratory droplets during direct and prolonged face-to-face contact is another way through which the disease can be transmitted, human-to-human transmission can also occur through direct contact with the body fluids of an infected person or with virus-contaminated objects, such as linens, bedding, or clothing [3]. Early symptoms of monkeypox diseasemay include fever, headache, muscle aches and backache, swollen lymph nodes, chills, and exhaustion [4],while the major symptom during the advanced stage of the disease is the development of rash, usually on the face or extremities or other parts of the body such as the hand, feet, mouth, and genitals [5].Severe cases of

monkeypox disease occur more commonly among children, depending on the extent of the virus exposure, patient health status and nature of complications. Complications of monkeypox can include secondary infections, bronchopneumonia, sepsis, encephalitis, and infection of the cornea with ensuing loss of vision [6]

The West and Central Africa are the regions of the world where the monkeypox virus is endemic [7], however, outbreaks and cases of the momeypoxdisease in humans keep occurring even outside these endemic regions [7]. In 2003, a human monkeypox case was reported in the United States of America (U.S.A.) and was traced to imported rodents from Ghana [8]. Recent outbreaks have been reported in the United Kingdom (U.K.), the U.S.A., Canada, France, Germany, Belgium, Spain, Portugal, Italy, Sweden, and Australia [9]. Thecauses and reasons for the spread of the disease in locations where it has never been reported before, equally call for global public health concern and action.Another public health concern is the non-availability of a widely used vaccine at the moment against the virus.The small pox vaccination had been proven to provide some protection against monkeypox [10], however, following the global eradication of smallpox in the 1980s, it vaccination ceased leavingthe population, especially those in the resource-limited endemic regions of the monkeypox virus susceptible to contracting the virus. This probably explains why repeated outbreaks in these regions and other new locations have been recorded. With enforcement of little or no preventive measures (quarantine of persons from endemic locations, use of face masks) by countries, outbreaks may spread to more locations thereby posing a threat human existence.

1.1 Objective

The objective of this paper is to review human monkeypox outbreaks globally and how these outbreaks constitute a threat to human existence.

2. METHODOLOGY

A review of literatures reporting outbreaks of monkeypox was conducted to identify all reported outbreaks.

2.1 Literature search strategy

There are two types of search strategies for literature: sensitive and specific [11]. The sensitive search deals with the number of relevant articles retrieved during a search. In contrast, the specific search concerns the number of irrelevant articles not retrieved during a search. The specific search is narrowed down to only articles relevant to the search term and may exclude other relevant articles. The sensitive search, on the other hand, retrieves a wider array of articles, thereby giving a high probability of getting all articles that are relevant for a study [11]. The sensitive search strategy was employed to retrieve all relevant articles to develop a full review. The search was conducted using appropriate keywords in PubMed and google scholar. In PubMed, for instance, searches included Medical Subject Headings (MeSH) and limits to title and abstract (tiab). The search string used in PubMed was Monkeypox[MeSH] OR "Monkeypox virus"[MeSH] OR monkeypox[tiab] OR “monkeypox” [tiab]. In google scholar search, search terms such as "monkeypox outbreaks" OR "outbreak of monkeypox in endemic countries" OR "recent outbreaks of monkeypox."

2.2 Screening of identified literature for eligibility and inclusion

After all, articles were identified from Pubmed and google scholar and, duplicateswere removed, the title and abstract screening were performed. Articles containing relevant data/information for the review objective, including outbreak reports, were selected for full-text screening. Excluded were non-human studies, modelling studies that did not provide information on disease outbreaks in humans, and articles with information that does not relate to the review aim or objective. In the event of doubt, the article was selected for full-text screening. Full-text articles were then reviewed to determine whether they met the review's aim. Some additional exclusions occurred in this step. For example, only one article was included for articles with similar results or information, usually the most recent. In some cases, there was a partial overlap of data or information, such that different articles included previously reported cases plus some new cases. In this instance, only the new cases in each article were included in the data extraction sheet which was created for eligible articles.

Case reports, outbreak investigations, epidemiological studies, and surveillance studies, were suitable for extraction from the literature searches. For these article types, no formal checklists for critical appraisal are available, so no formal quality assessments were performed. Information on study quality reported by the selected articles' authors was added as comments in the data extraction sheet. In addition to PubMed and google scholar searches, other sources of grey literature were also searched. These include websites of the World Health Organization (WHO), specifically a review of the Weekly Bulletins on Outbreaks and Other Emergencies,

United States Centres for Disease Control and Prevention (C.D.C.), Africa C.D.C., Nigeria C.D.C., African Field Epidemiology Network, Epicentre, and ProMed. The relevant information from this grey literature was also added to the data extraction sheet.No limit was applied to the searches in terms of date since the topic of interest is dates far back to 1970. The limit was, however, applied to language as only articles reported in English were retrieved.

2.3 Data synthesis and reporting

Data/information from individual studies and literature included in the review were reported using a tabular format. The use of tables for reporting was informed by its ability to summarize lengthy information with significant visual appeal, making the results more easily understandable and thus more attractive to the users.

2.4 Case definition

Since the review focused on the monkeypox outbreak, the following case definitions were used.

Suspected case: Sudden onset of high fever, followed by a vesicular-pustule eruption presenting predominantly on the face, palms of the hands, and soles of the feet; or the presence of at least five (5) smallpox-type scabs

Confirmed case: A suspected case with laboratory confirmation; Positive IgM (Immunoglobulin M) Antibody, Polymerase chain reaction (PCR), or virus isolation.

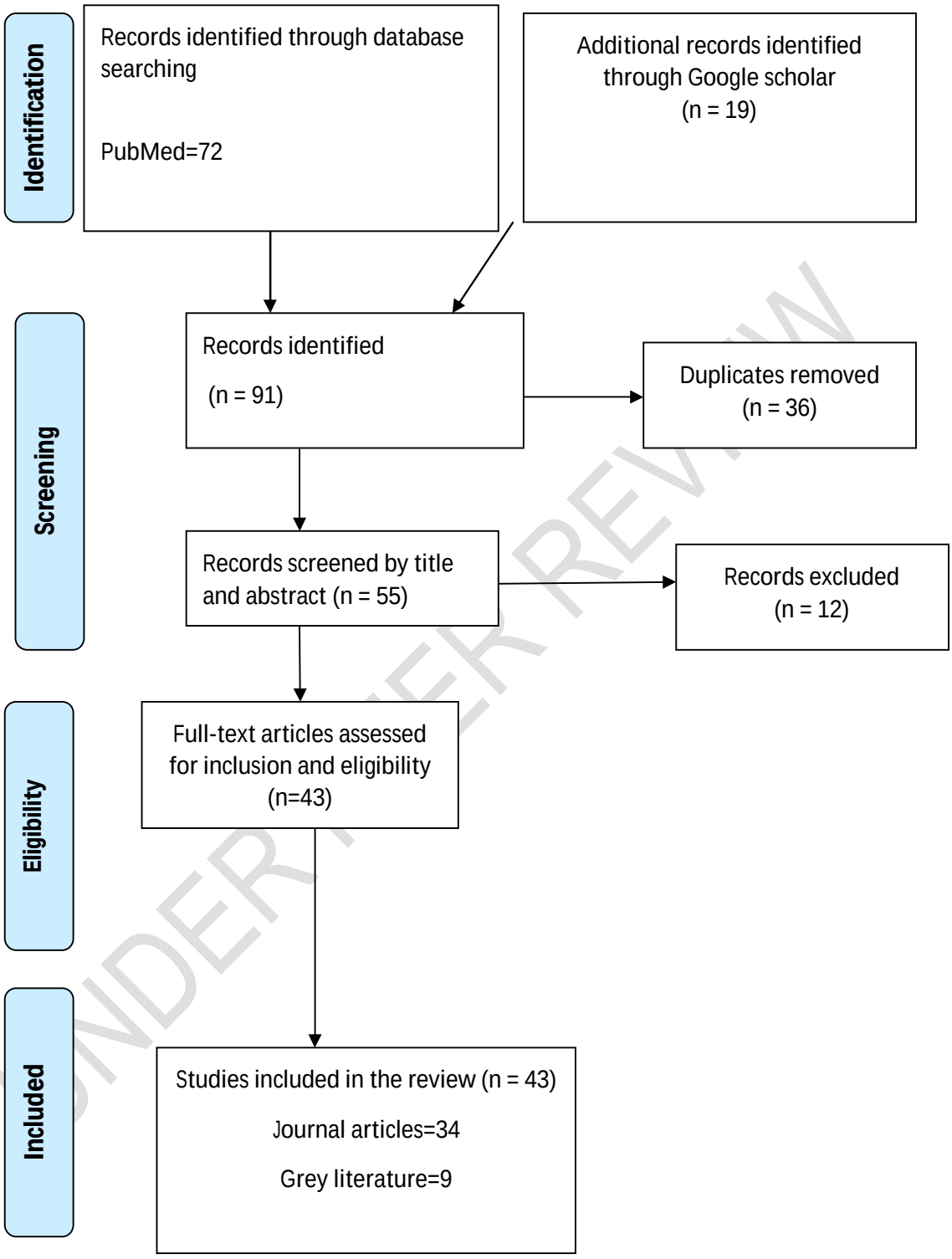
Probable case: A suspected case with no possibility of laboratory confirmation but with an epidemiological link to a confirmed case.

Possible case: Vesicular, pustular, or crusted rash, not diagnosed as chickenpox by the family or the healthcare provider, or History of fever and vesicular or crusty rash,

or Individual met one of the epidemiologic criteria or demonstrated elevated levels of orthopoxvirus specific IgM and had unexplained rash and fever and two(2) other signs or symptoms from the clinical criteria.

3. RESULTS

The search strategy yielded a total of Ninety-one (91) publications, fifty-five (55)of which were selected for full-text screening after identifying and removing thirty-six (36) duplicate records. Of these, forty-three (43) articles were suitable for data extraction, thirty-four (34) Journal articles, and nine (9) grey literature. The PRISMA flowchart of the systematic review selection process is shown in Fig 1.



3.1 Description of included studies and literatures

All the forty-three (43) included studies/literatures reported on data/cases (suspected, confirmed, probable, and or possible) of monkeypox in various countries from 1970 to 2022.

3.2 Number of cases per country per outbreak

Since the discovery of the first case in D.R.C. in 1970, there has been a resurgence of outbreaks in the country, neighboring Central and western African countries, and even countries outside the African continent. Table 1 below summarizes outbreaks in various countries as of May 23, 2022. The data extraction sheet contains the detailed number of cases per country per outbreak[refer to the Supplementary information].

Table 1: Summary of outbreaks and cases

S/N	Country	Episodes of outbreak (Years)	Total suspected cases	Total confirmed cases	Total death cases
1	Democratic Republic of Congo	14 (1970-2022)	10,036	1,405	127
2	Gabon	1 (1987)	NR	4	2
3	Ivory Coast (Côte d'Ivoire)	2 (1972, 1981)	NR	2	0
4	Central African Republic	10 (1980-2022)	138	67	5
5	Congo	5 (2003-2019)	162	45	6
6	Sierra Leone	3 (1970, 2014, 2017)	NR	3	0
7	Cameroon	4 (1989, 2018, 2019, 2022)	62	6	2
8	Nigeria	5 (1971-2022)	322	140	8
9	South Sudan	1 (2005)	49	19	0
10	Liberia	2 (1970, 2017)	16	6	0
11	USA	2 (2003, 2022)	96	49	0
12	UK	3 (2018-2022)	NR	23	0

13	Portugal	1 (2022)	NR	23	0
14	Spain	1 (2022)	62	14	0
15	Belgium	1 (2022)	NR	4	
16	Germany	1 (2022)	2	1	0
17	France	1 (2022)	3	1	0
18	Italy	1 (2022)	2	1	0
19	Sweden	1 (2022)	NR	1	0
20	Netherlands	1(2022)	NR	1	0
21	Austria	1(2022)	NR	1	0
22	Canada	1(2022)	20	2	0
23	Australia	1(2022)	NR	2	0
24	Israel	2 (2018, 2022)	NR	2	0
25	Swizerland	1 (2022)	NR	1	0
26	Singapore	1 (2019)	NR	1	0

Major findings

Overall, 10,970 suspected cases of human monkeypox have been reported across 26 countries since from 1970 to May 2022. 1,824 of these cases were confirmed, while 146 deaths have been recorded. The highest outbreaks occurred in D.R.C. (14) and the Central African Republic (10). The highest mortalities were from D.R.C. (127) and Nigeria (8). Most of the cases outside Africa were the first cases in such countries which were all traced to travel histories to endemic locations or regions. The first monkeypox reported outside Africa was in 2003 when an outbreak of 47 confirmed or probable cases occurred in the U.S.A. following exposure to infected pet prairie dogs, which had acquired monkeypox virus from infected exotic animals imported from Ghana [12]. Since then, several cases have been reported in different countries outside Africa, as reported in the current (2022) outbreak. Reasons for current monkeypox outbreaks are still linked to travel history to endemic regions or

importation of infected animals from these regions. The spread of the outbreak to different locations and countries, though with few cases, fatalities could in the future be a threat to humans and, therefore, a growing public health concern.

4. DISCUSSION

This review provides a detailed chronicle of monkeypox outbreaks since its first case was identified over five decades ago. The repeated outbreaks and high case fatality rates recorded in D.R.C., C.A.R., and Nigeria indicate weak health systems and poor epidemic preparedness and response. [13] asserted that Africa has one of the weakest health systems globally and consequently limited preparedness and response to disease outbreaks, epidemics, and pandemics. This is evident in the frequency of outbreaks and the number of monkeypox cases recorded in most African countries compared to Western countries. For instance, in the U.S.A., after the first outbreak in 2003, in which 47 cases were confirmed, the outbreak resurged after 19 years (2022) with two confirmed cases; this implies a robust health system with adequate disease outbreak preparedness and response. This is unlike in most of the African countries, in Nigeria for instance, apart from the frequent outbreaks (2018, 2022), the number of confirmed and probable cases has escalated as well, from 3 cases in the 1970s to 137 cases in 2017–2022. In the D.R.C., the frequency of outbreaks is yearly (2020, 2021, and 2022), a similar situation is reported in C.A.R. as the outbreak was reported in 2016, 2017, 2019, and 2022.

The geographical spread of the monkeypox, especially during the recent (2022) outbreak, is also a call for concern. Over the past 5 decades, monkeypox outbreaks have been reported in 26 countries. From 2003, cases of monkeypox have occurred

outside of Africa and have continued to spread. The first reported case outside Africa was in the United States of America (U.S.A.)in 2003, traced to infected rodents from Ghana, imported into the U.S. This led to animal-to-animal transmission and subsequently animal-to-human transmission, ultimately resulting in an outbreak of 47 confirmed or probable cases. Due to trans-border human movement and activities, significant human-to-human transmission has been reported in C.A.R.[14], D.R.C.[15], Nigeria [16] in the U.K. [17]. This poses a severe threat to the fast spread of the disease. Mathematical modeling of human-to-human transmission found that monkeypox has epidemic potential, with R0 >1 [18].

The absence of a widely used vaccine against monkeypox could also be one of the reasons for the surge in the outbreaks since the population is susceptible. Smallpox vaccination was proven to be approximately 85% protective against monkeypox[19]. However, after the successful vaccination campaign against smallpox, the disease was declared eradicated in 1980 by the World Health Assembly. Consequently, its routine vaccination was ceased [20]. Other reasons for the surge in the outbreaks could be deforestation and rapid urbanization, especially in Africa,promoting wildlife-human contact, a risk factor for monkeypox. [21] showed that global disease outbreaks indirectly affect the population health, resulting in the diversion of limited resources towards their management. Hence the need to put in place sustainable measures that will mitigate against their occurrence and spread. The lack of these measures has resulted largely in the appearance of new cases outside of Africa and other non-endemic African countries, thus highlighting the risk for geographical

spread and the global relevance of the disease. Given the current environment for pandemic threats, the public health importance of monkeypox disease should not be underestimated. International support for increased Surveillance and Detection of monkeypox cases,especially in resource-limited endemic regions, are essential for understanding the continuously changing epidemiology of this resurging disease.

In summary, monkeypox could pose a threat to human existence given that there is no measure currently (widely used vaccination, quarantine measures to curb trans-border transmission, measures to contain human-to-human and animal-to-human transmission) to prevent its outbreaks and spread

4. CONCLUSION

Monkeypox has continued to resurge and even spread to new regions and countries over the decades with little or no vaccination interventions to tame it. The human population is susceptible, especially in the absence of vaccination intervention; human-to-human transmission is also an enhancing factor for the spread of the disease, especially with little or no quarantine measures currently in place, as was the case with Coronavirus Disease 2019(COVID-19).Therefore, it can be concluded that if no urgent measures are taken, the increased geographical spread of the disease would be recorded in no distant time, which would pose a threat to human existence.

5. Recommendations

To avert the looming threat posed by the widespread outbreaks of the monkeypox disease, this study made the following recommendations;

i. Resource-limited endemic regions should be supported by the international community to increase surveillance and detection of

monkeypox cases. This would go a long way in curbing transmission of the disease as detected cases would be appropriately managed hence curbing domestic and trans-border transmissions.

ii. The populace in the virus endemic regions should be given proper health education regarding handling and consumption of animals.

iii. Travelers from the virus endemic regions should be quarantine upon arrival to other countries. This would check most of the trans-border transmissions.

iv. Movement of animals and pets should be closely monitored by relevant health authorities of countries in order to ensure that infected animals are not moved from one place to another thereby spreading the virus.

6Strengths and limitations

The strength and limitations of this review are discussed below.

Strengths: one of the significant strengths of this review is that rigorous review methods such as the PRISMA guidelines were employed and strictly adhered to. This guideline led to a broad search strategy on monkeypox worldwide, without a time limit, which reduced selection bias. In addition, there was a thorough review of the grey literature. Overall, 43 relevant sources were identified for comprehensive data extraction, producing a robust review.

Limitations: The number of confirmed, probable, and/ or possible cases and case fatalities reported by included studies/literatures and presented in the review may likely not be the actual figures as Disease Surveillance and Response systems in most African countries are weak. For instance, in the D.R.C., WHO supported

monkeypox surveillance. However, this support was withdrawn in 1986, probably leading to poor Surveillance and consequently under-reporting of cases for outbreaks that occurred after 1986. The literature search for the review was limited by language, thus depriving the inclusion of relevant studies (published in other languages other than English), which could have added to the quality of the review.

7. Abbreviations

PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses

D.R.C.: Democratic Republic of Congo

C.A.R.: Central African Republic

MesH: Medical Subject Headings

WHO: World Health Organization

C.D.C.: Centre for Disease Control

PCR: Polymerase Chain Reaction

IgM: Immunoglobulin M

U.S.A: United States of America

U.K: United Kingdom

COVID-19: Coronavirus Disease 2019

CONSENT (WHEREEVER APPLICABLE)

Not applicable

ETHICAL APPROVAL (WHEREEVER APPLICABLE)

Not applicable

DISCLAIMER

The view expressed in the articles is those of the author and not that of the affiliated institution.

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