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Monkeypox cases: Emerging infectious disease, risk factors and diagnosis

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Abstract

Emerging viral disease is a public health concern, with potential hazard for human, animal and environmental health. Forty years ago, after the eradication of smallpox in Nigeria, emerging zoonotic Orthopoxviruses such as monkeypox viruses continue to infect human together with wild and domestic animals. Currently, the geographical distribution of monkeypox virus in a wide range of host's worldwide raises major concerns regarding the possibility of outbreak from endemic regions to non-endemic regions. A systematic literature review was conducted in PubMed and Google scholar databases using the search terms: monkeypox, endemc region, non-endemic region and risk factors. Here, we review the global host ranges and current epidemiological surveillance. It reveals the immigrants' influx from viral dissemination regions to new geographical regions is the one of the risk factors that attributes to recent outbreak of monkeypox cases worldwide. In addition, the most of individuals below forty years in Nigeria come down with monkeypox cases because they lack protective immune coverage within the communities.

Keywords: Monkeypox virus; Zoonosis; Endemic; Non-endemic; Risk factors

1. Introduction

Monkeypox is a viral zoonosis disease associated with negative effect on human and animal health [1], with symptoms similar to those seen in the past in smallpox patients, although it is clinically less severe. Despite the eradication of smallpox over forty years ago, and subsequent cessation of smallpox vaccination, monkeypox has emerged as the most important orthopoxvirus for public health [2]. Monkeypox primarily occurs in central and west Africa, often in proximity to tropical rainforests, and has been increasingly appearing in urban areas [2]. Monkeypox is caused by monkeypox virus, a member of the Orthopoxvirus genus in the family Poxviridae [3]. This is mainly found in remote Central and West African communities, close to tropical rain forests [3]. In 2017, the reemergence of monkey pox virus is reported at Bayelsa state and over 39 years ago, there was no reported cases of this disease in Nigeria, before the travelers export it from Nigeria to various parts of the countries between 2018 and 2019 respectively [4]. In addition, genome-wide phylogenetic studies reveal that monkeypox virus (MPXV) isolates from recent 2017 outbreak in Nigeria are monophyletic with the isolate exported to Israel from Nigeria, but do not observe any share common ancestor with those isolates obtained from earlier outbreaks in 1971 and 1978 respectively [4]. However, smallpox vaccine provided effective protection against smallpox virus and monkeypox virus respectively, but the absence of smallpox virus lower the population-wide immunity coverage during this eradication efforts, and increases the re-emergence of Monkey pox virus infection [5; 6].

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2. Material and methods

2.1. Risk factors

Monkeypox virus is an enveloped double-stranded DNA virus that belongs to the *Orthopoxvirus* genus of the *Podxviriae* family [7]. There are two distinct genetic clades of the monkeypox virus: the central African (Congo Basin) clade and the West African clade. The Congo Basin clade has historically caused more severe disease and was thought to be more transmissible [7]. The geographical division between the two clades has so far been in Cameroon, the only country where both virus clades have been found [6].

Animal-to-human (zoonotic) transmission can occur from direct contact with the blood, bodily fluids, or cutaneous or mucosal lesions of infected animals [6]. In Africa, evidence of monkeypox virus infection has been found in many animals including rope 8], squirrels, tree squirrels, Gambian poached rats, dormice, different species of monkeys and others [9]. The natural reservoir of monkeypox has not yet been identified, though rodents are the most likely [9]. Eating inadequately cooked meat and other animal products of infected animals is a possible risk factor [10]. People living in or near forested areas may have indirect or low-level exposure to infected animals.

Human-to-human transmission can result from close contact with respiratory secretions, skin lesions of an infected person or recently contaminated objects [11]. Transmission via droplet respiratory particles usually requires prolonged face-to-face contact, which puts health workers, household members and other close contacts of active cases at greater risk [12]. However, the longest documented chain of transmission in a community has risen in recent years from 6 to 9 successive person-to-person infections [13]. This may reflect declining immunity in all communities due to cessation of smallpox vaccination [13] (Table 1).

Table 1 Risk factors associated with monkeypox cases in endemic regions

Risk factors for monkeypox	Authors
Age	In Nigeria, most people suffered from monkeypox are less than 40 years and lack cross-protective immunity because they were given birth after discontinuation of the smallpox eradication campaign Petersen et al., [10].
Nosocomial infection	Healthcare-associated transmission Petersen et al., [12].
Zoonotic infection	Interaction with infected prairie dogs Kile et al., [9], infected wildlife bites from peri-domestic animals, hunters Meslikn et al.,[13]; Reynolds et al.,[21]; Household materials Quiner et al.,[14]; Yinka-Ogunleye et al.,[8]; Guagliardo et al.,[7], Peridomestic rodents Reynolds et al., [27]; Salzer et al.,[15].
Travellers	Immigrants to non-endemic monkeypox Alakunle et al.,[4]
Human to human transmission	Inter human transmission Nolen et al.,[11]

2.2. Endemic and non-endemic countries

Since then, most cases have been reported from rural, rainforest regions of the Congo Basin, particularly in the Democratic Republic of the Congo and human cases have increasingly been reported from across central and West Africa[11].
Since 1970, human cases of monkeypox have been reported in 11 African countries: Benin, Cameroon, the Central African Republic, the Democratic Republic of the Congo, Gabon, Cote d'Ivoire, Liberia, Nigeria, the Republic of the Congo, Sierra Leone and South Sudan [14; 10; 8; 7]. For example, in 1996–1997, an outbreak was reported in the Democratic Republic of the Congo with a lower case fatality ratio and a higher attack rate than usual [14]. A concurrent outbreak of monkeypox was found, which could explain real or apparent changes in transmission dynamics in this case, where most of the travellers are the main vehicle for the sharing of this virus to non-endemic areas [4]. Since 2017, Nigeria has experienced a large outbreak, with over 500 suspected cases and over 200 confirmed cases and a case fatality ratio of approximately 3%. Cases continue to be reported until today [6]. The major mode of transmission of this virus could attribute to animals to human interaction within this endemic regions [13; 9]. Recent report shows that the highest cases of monkeypox in Africa was found in Democratic Republic of the Congo followed by Nigeria and Cameroon

whereas Central African Republic recorded the least cases of monkeypox [6; 7] (Figure 1). Nigeria Center for Disease Control and Prevention (NCDC) reports the monkeypox cases in Nigeria from September 2017 to February, 28th, 2022 as follows: Rivers State topped the list with 23% cases, followed by Bayelsa and Lagos States with 19% and 14% cases respectively. While the Federal Capital Territory (FCT) recorded 3% cases, the other states are Delta (13%), Cross River (6%), Edo (5%), Imo (4%), Akwa Ibom (3%), Oyo (3%), Enugu (2%), Abia (1%), Plateau (1%), Nasarawa (1%), Benue (1%), Anambra (1%), Ekiti (1%), Ebonyi (0%), Niger (0%), Ogun (0%) and Adamawa (0%)(Figure 2).

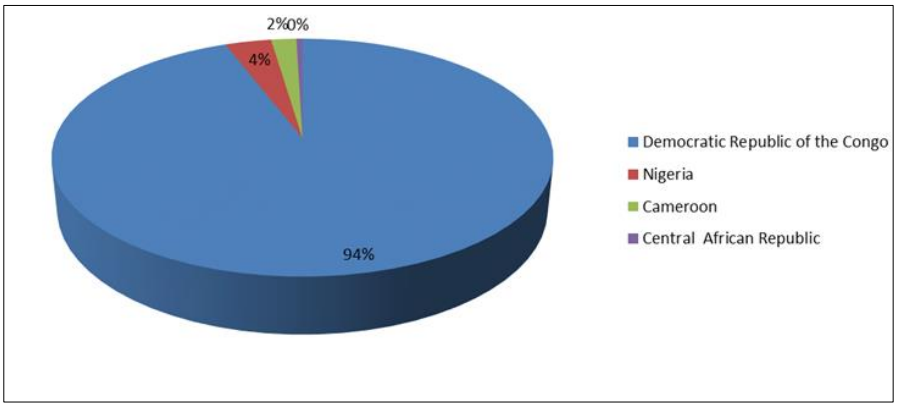

Figure 1 Prevalence cases of monkeypox in endemic countries between 15th December, 2021 to 1 may, 2022[6]

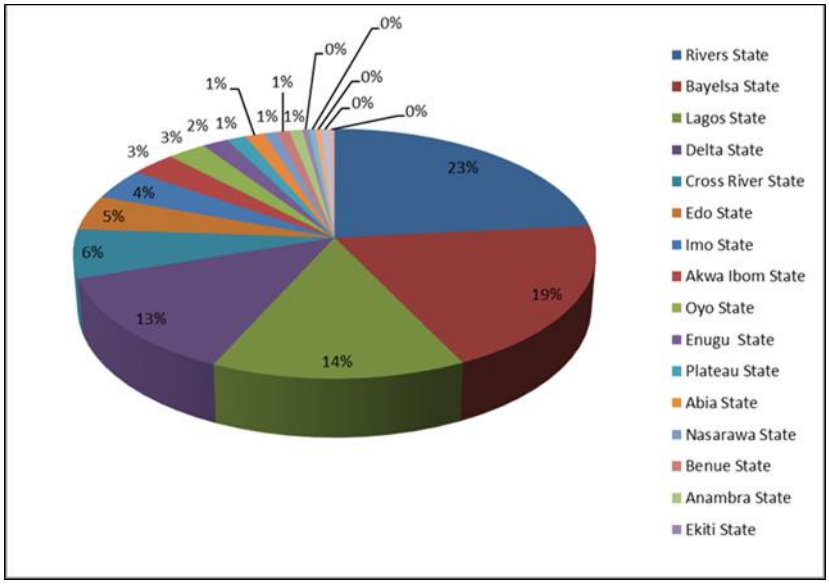

Figure 2 Nigeria Center for Disease Control and prevention reports the monkeypox cases from september 2017 to february, 28th, 2022 [6]

Monkey pox is a disease of global public health importance as it not only affects countries in west and central Africa, but the rest of the world [21]. In 2003, the first monkeypox outbreak outside of Africa was in the United States of America and was linked to contact with infected pet prairie dogs [9; 21]. These pets had been housed with Gambian pouched rats and dormice that had been imported into the country from Ghana. This outbreak led to over 70 cases of monkeypox in the U.S. Monkeypox has also been reported in travelers from Nigeria to Israel in September 2018, to the United Kingdom in September 2018, December 2019, May 2021 and May 2022, to Singapore in May 2019, and to the United States of America in July and November 2021. In May 2022, multiple cases of monkeypox were identified in several non-endemic countries. Studies are currently underway to further understand the epidemiology, sources of infection, and transmission patterns [26]. Recently, 92 molecular confirmed cases, and 28 presumptions diagnose of monkeypox cases has been recorded in 12 Member States that are non-endemic for monkeypox virus [26]. The Portugal, Spain and United Kingdom recorded the highest cases of monkey pox while other countries reported low cases of monkey pox (figure3). The Canada reported the highest suspected cases of monkeypox followed by Spain whereas Belgium and France recorded the lowest suspected cases of monkeypox [26] (figure 4).

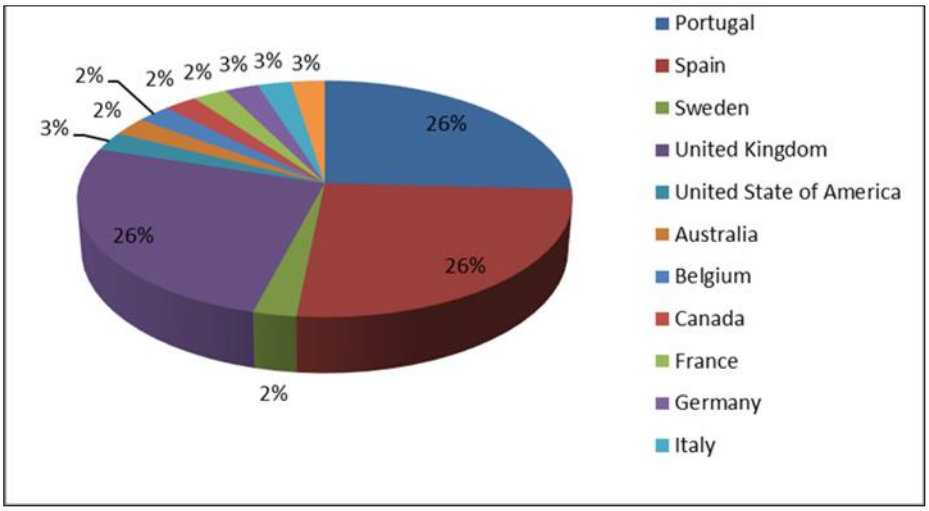

Figure 3 Prevalence of monkey pox cases in non-endemic countries reported to WHO between 13-21st, May, 2022

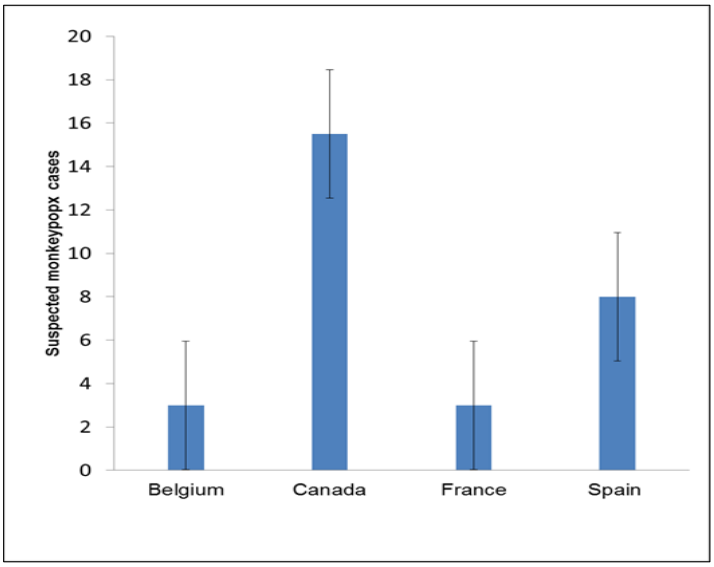

Figure 4 Proportion of suspected cases in non-endemic countries reported to WHO between 13-21st, May, 2022 [26].

3. Results and discussion

3.1. Investigation

The clinical differential diagnosis that must be put into consideration includes other rash illnesses, such as chickenpox, measles, bacterial skin infections, scabies, syphilis, and medication-associated allergies [16]. Lymphadenopathy during the prodromal stage of illness can be a clinical feature to distinguish monkeypox from chickenpox or smallpox [16]. If monkeypox is suspected, health workers should collect an appropriate sample and have it transported safely to a laboratory with appropriate capability [17]. Confirmation of monkeypox depends on the type and quality of the specimen and the type of laboratory test. Thus, specimens should be packaged and shipped in accordance with national and international requirements [17]. Polymerase chain reaction (PCR) is the preferred laboratory test given its accuracy and sensitivity (Table 2). For this, optimal diagnostic samples for monkeypox are from skin lesions – the roof or fluid from vesicles and pustules, and dry crusts [18]. Where feasible, biopsy is an option. Lesion samples must be stored in a dry, sterile tube (no viral transport media) and kept cold. PCR blood tests are usually inconclusive because of the short duration of viremia relative to the timing of specimen collection after symptoms begin and should not be routinely collected from patients [18]. As orthopoxviruses are serologically cross-reactive, antigen and antibody detection methods do not provide monkeypox-specific confirmation [8]. Serology and antigen detection methods are therefore not recommended for diagnosis or case investigation where resources are limited [8]. Additionally, recent or remote

vaccination with a vaccinia-based vaccine (e.g. anyone vaccinated before smallpox eradication, or more recently vaccinated due to higher risk such as orthopoxvirus laboratory personnel) might lead to false positive results. In order to interpret test results, it is critical that patient information be provided with the specimens including: a) date of onset of fever, b) date of onset of rash, c) date of specimen collection, d) current status of the individual (stage of rash), and e) age [26].

Table 2 Molecular diagnosis of Monkeypox virus

Investigations	Authors
Polymrase Chain Reaction(PCR)	West African Monkeypox Virus was identified, United Kingdom (n= 1) and, Singapore (n =1), among travellers from Nigeria Mauldin et al.,[19]
PCR and Ig M antibodies	122 confirmed cases with real-time PCR and Orthopoxvirus IgM antibodies including 7 deaths in Nigeria Yinka-Ogunleye et al., [8].
Taq man-based assay	13 confirmed cases in 2003 US outbreak Li et al.,[20]
PCR	Monkeypox's pox traveller from Singapore to Surabaya, Indonesia Tumewu et al., [22].
PCR	From 2010 – 2019, the incidence of Clades-Central African and West African monkey pox virus are 10.6% (95% Cl: 8.4%-13.3%) versus 3.6% (95% Cl: 17%-6.8%) respectively Bunge et al., [22]; Bricaire and Bossi, 2006).

4. Conclusion

Surveillance and rapid identification of new cases is critical for outbreak containment. During human monkeypox outbreaks, close contact with infected persons is the most significant risk factor for monkeypox virus infection. Health workers and household members are at a greater risk of infection. Health workers caring for patients with suspected or confirmed monkeypox virus infection, or handling specimens from them, should implement standard infection control precautions. Clinical care for monkeypox should be fully optimized to alleviate symptoms, manage complications and prevent long-term sequelae. Patients should be offered fluids and food to maintain adequate nutritional status. Secondary bacterial infections should be treated as indicated. An antiviral agent known as tecovirimat that was developed for smallpox was licensed by the European Medicines Agency (EMA) for monkey pox in 2022 based on data in animal and human studies. It is not yet widely available.

Compliance with ethical standards

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Authors 'Contribution

All authors contributed to preparing, review and editing of the article. All authors read and approved the final version of the manuscript.

Disclosure of conflict of interest

The authors declare that there are no conflicts of interest of this article.

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