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Recently spreading human monkeypox virus infection and its transmission during COVID-19 pandemic period: A travelers' prospective

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ABSTRACT

Presently, monkeypox has emerged in multiple countries with many confirmed cases, posing a global public health threat. A link has been found between air travel and the international spread of infectious diseases including the previous spread of monkeypox.

This article highlights the spread of COVID-19 through air travel, and then monkeypox spread from one country to another. Scientists are trying to establish the air travel and monkeypox spread. Any travel link from an endemic country has not been proven yet to describe the rising number of current monkeypox cases in non-endemic countries. Due to the quantification method, the direct link of the diseases with air travel might be difficult to establish. However, we have also developed different statistical models of the confirmed cases and the number of air travelers per year (noted in countries where monkeypox has spread). As there is no direct link, these models might show a probability of an indirect association of air travel. However, more strong evidence is needed in this direction.

Although, the sudden appearance of monkeypox cases in multiple countries in a few days demands comprehensive epidemiological investigations, genome sequencing, and phylogenetic analysis of viral isolates to prove the travel link from an endemic country. At the same time, it is also necessary to know the real cause while also exploring any direct and/or indirect travel links between different countries. Similarly, the possibility of any zoonotic event should find out to understand the more about natural animal reservoir(s) for the monkeypox virus, which is unknown until now. However, this report will help researchers for conducting further explorative research and investigations for understanding transmission patterns and guide policymakers to make proactive policies to limit the spread of monkeypox.

Various emerging infectious virus disease outbreaks with zoonotic origin have occurred in recent years such as SARS-CoV-2, MERS-CoV, H7N9 (highly pathogenic avian influenza), Ebola virus, Chikungunya virus, Dengue Virus, and Japanese encephalitis virus, which are highly pathogenic in nature [1–3]. It was observed that these viruses are spread by international travelers from time to time. One most recently re-emerging zoonotic diseases is monkeypox [4].

An uncommon and life-threatening viral disease, monkeypox has been recently detected in more than 12 non-African countries. WHO has confirmed more than 123 cases of monkeypox (both suspected or confirmed cases) from countries viz., Australia, Belgium, Canada, France, Germany, Italy, Netherland, Portugal, Spain, Sweden, the UK, and the USA (Fig. 1a; Fig. 1b) [5]. The highest number of cases (21–30) has been reported from Portugal, Spain, and the UK (Fig. 2). Recently, a report informed that it might be community transmission in the UK [6]. However, from the literature search, we found that most cases of human monkeypox, which have been reported from time to time, are observed in West Africa and Central Africa that are endemic regions for this virus.

This zoonotic virus was first detected in 1958 in the monkey colonies, which were preserved in a Danish research laboratory, and pox-like disease was observed. Therefore, the condition was named as 'Monkeypox.' However, this detection of monkeypox case was from an animal. The first human case was reported when the virus was identified in a child from Congo (DRC) in 1970 [5–9]. Monkeypox virus belongs to

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the genus *Orthopoxvirus* and is a member of the family Poxviridae. Two clades are noted in this virus: one is the Congo Basin clade (also entitled as Central African clade), and the other is the West African clade. The virus contains double-stranded DNA (dsDNA), and the genome sequence length is about 1,97,124 bp.

Several researchers have reported that air travel is the source of the spread of infectious diseases [10,11]. Currently, due to the increase of the global population, transportation networks have increased. Air travel has played a significant role among transportation networks. Due to the increasing affordability and effortlessness, air travel has created faster mobility for people. It has been recorded that more than one billion travelers travel by air yearly. At the same time, it is noted that, in developing countries, more than fifty million travelers travel by air annually [11,12]. Likewise, among air travel, more than 40% of the air traveler traveled from the international air travel. However, owing to air travel and mobility of people, different zoonotic infectious diseases, vector-borne, food-borne, and air-borne diseases have been reported to be transmitted during air travel [11]. Tuite et al. have observed that most infectious diseases spread from one country to another through international air travel. However, significantly increased air travel has been observed over the past decade [13]. At the same time, another group of researchers has noted that mobility is a significant cause of spread of infectious diseases. They have developed multiscale mobility models and describe how multiscale mobility is related to disease dynamics [14]. The global spread of the COVID-19 from China or country to country is a significant example of spread by the international travelers through the air travel.

International travel has played an immense role in spreading the SARS-CoV-2 virus from country to country (Table-1). In China, travel restrictions were enforced during COVID-19 times to limit the spread of

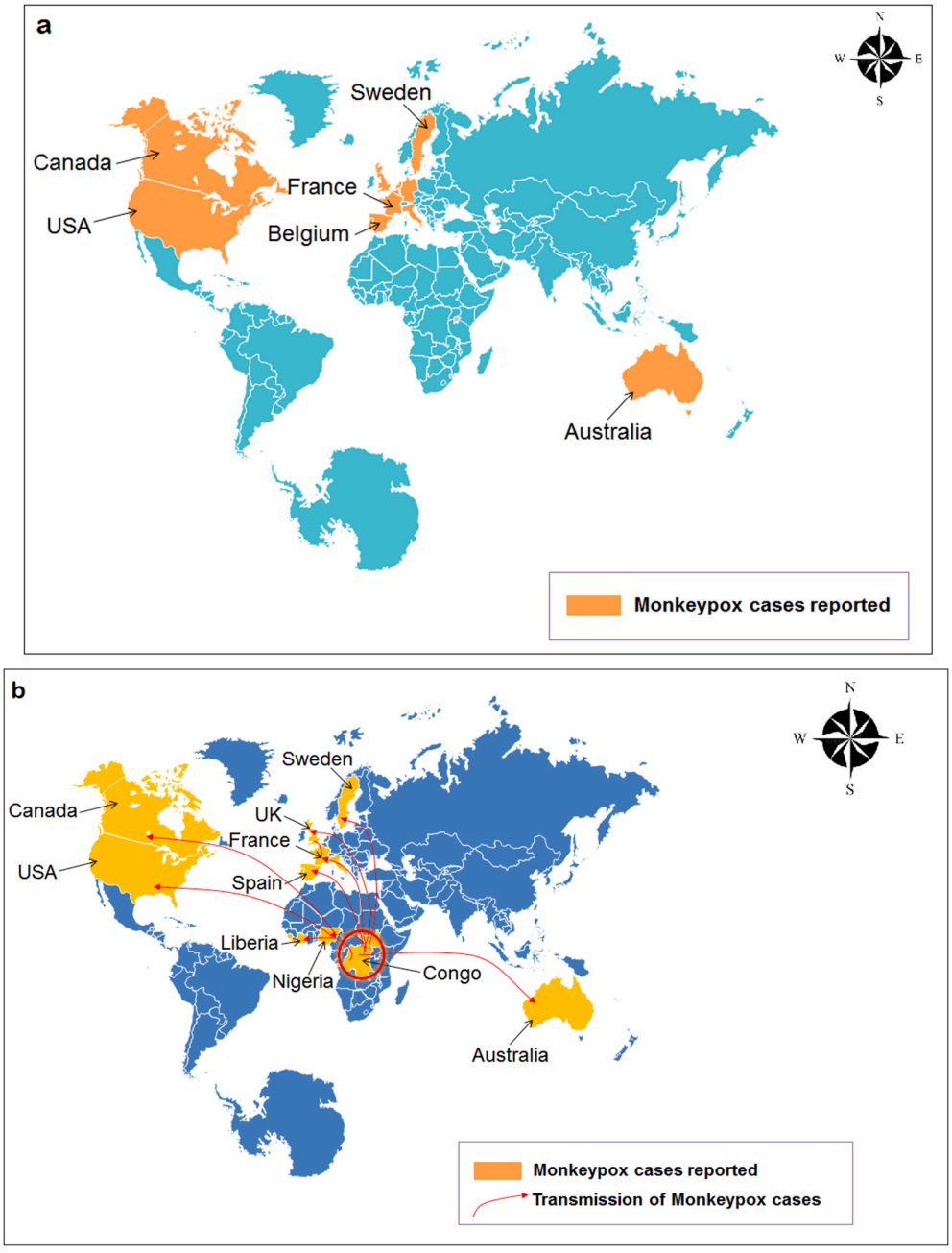

Fig. 1. Recent monkeypox outbreaks and the disease reporting non-African countries where the outbreak is being experienced (a) recent monkeypox outbreak in non-African countries and their geographic locations (b) recent monkeypox transmission route in non-African countries.

the disease. At the same time, border control measures were imposed in several other countries from time to time to control the outbreak. Wells et al. have observed that lockdowns reduced the rate of disease exportation by 81% compared to border control measures [15]. Several other researchers have developed a model to understand the consequence of travel restrictions on the COVID-19 spread. In this direction, Chinazzi et al. developed a model to illustrate the outcome of travel restrictions during the COVID-19 and its effect on the spread of the disease. The model was calibrated using worldwide reported cases. It was noted that the travel ban was implemented in Wuhan on January 23, 2020. At the same time, they have also indicated that many infected travelers from different Chinese cities modeling results showed that travel restrictions (to China or from China) in mainland facilitated a 50% or higher reduction of transmission of the diseases [16]. Likewise, Burns et al. tried to comprehend the outcome of travel restrictions on transmitting the diseases. They have described several factors associated with the

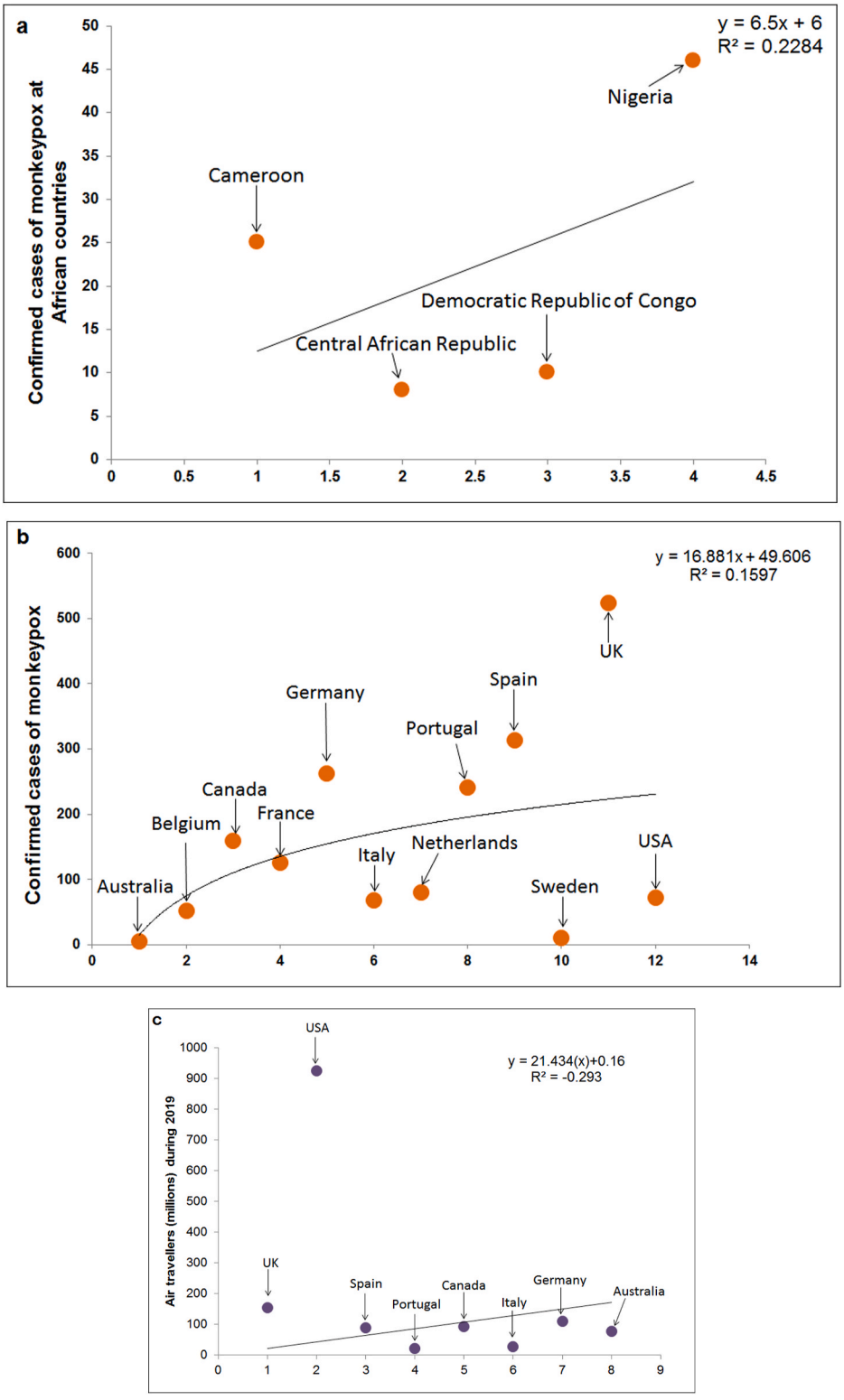

Fig. 2. Developed statistical models for recent monkeypox outbreak (a) one regression model was developed using the number of infected cases in African countries for the recent monkeypox outbreak. The model was developed using WHO open data from the WHO report published on June 17, 2022. (b) one regression model was developed using the number of infected cases in non-African countries for the recent monkeypox outbreak. The model was developed using WHO open data from the WHO report published on June 17, 2022. (c) one regression model was developed using the number of air travelers per year in non-African countries where recent monkeypox outbreaks are occurring. Data was collected from an open-source database (Statista). We collected the year 2019 data. After that, the pandemic started, and most of the air travel was stopped.

Table-1
Examples of SARS-CoV-2 spread through the air travel by travelers.

Sl. No.	COVID-19 spread by air travel (name of the countries)	Year of spread	Remark	Reference
1.	Wuhan, China to Thailand	January 2020	Researchers reported two cases of COVID-19 which was confirmed with genome sequencing and RT-PCR	[28]
2.	UK to Vietnam	March 2020	Transmission and increased infection risk of COVID-19 performed by epidemiological investigations	[29]
3.	Italy to South Korea	March 2020	Asymptomatic transmission of COVID-19 on an aircraft is an inadequate condition	[30]
4.	China to Greece	January 2020	Increased risk of in-flight transmission of COVID-19 causing virus for possibility of airborne spread, transmissibility includes the long incubation period	[31]
5.	Wuhan, China to Singapore	January 2020	The asymptomatic infection that was overlooked by simply symptomatic surveillance, whereas the actual COVID-19 infection might be higher.	[32]
6.	Israel to Greece	March 2020	Probable in-flight transmission of COVID-19 due to the close contact with the index case in Greece	[31]
7.	Central African Republic to France	March 2020	The easiest mode of SARS-CoV-2 transmission by travel together with their human carriers, and spreading of the virus on board	[33]
8.	Israel to Germany	March 2020	From the throat swab sample of passenger the presence of SARS-CoV-2 confirmed by RT-PCR	[34]

transmission consequence, such as travel volume levels, community transmission, etc. Similarly, Costantino et al. described the outcome of partial or complete travel bans from China to the spread COVID-19 in Australia [17]. However, it was noted that the proper research planning on early travel bans might be a control measure for any infectious disease like the COVID-19 pandemic.

In the case of monkeypox in the present scenario, there are no established travel links to endemic areas [5]. Au et al. have attempted to assess the potential pathways of commercial air travel and its transportation of the virus from endemic to non-epidemic regions for the current monkeypox outbreak [18]. During the earlier monkeypox virus infection cases in 1970, a link was established between travel cases of the disease to Africa or infected animals' import. Thereafter, in several previous cases, monkeypox transmission was investigated by the researchers from time to time [19], and in all the cases, air travel has been found to be a significant cause of the disease transmission (Table-2). However, Vaughan et al. have reported that two monkeypox virus infected cases were detected in persons who traveled from Nigeria to the South West England, UK [20]. Similarly, Erez et al. identified one case of monkeypox in Israel in 2018, and the case was imported from Nigeria to Israel. The swabs sample was collected to confirm the monkeypox virus, which were checked by a series of analyses such as PCR, ELISA, tissue culture, transmission electron microscopy, and immunofluorescence assays [21]. In July 2021, one traveler traveled from Nigeria to Texas (Dallas) and was recognized as the monkeypox virus-infected case, presented with all the clinical symptoms such as fatigue, cough, and fever. Whole-genome sequencing confirmed the monkeypox virus strain

Table-2
Examples of the monkeypox virus spread in non-African countries through air travel.

Sl. No.	Monkeypox spread by air travel (name of the countries)	Year of spread	Remark	Reference
1	From Nigeria to UK	September 2018	Two cases monkeypox were diagnosed in South West England who were traveled from Nigeria to the UK	[17]
2	From Nigeria to Singapore	May 2019	One Nigerian were diagnosed as monkeypox infected after two days of arrival in Singapore	[17]
3	From Nigeria to Israel	October 2018	38-year individual Israel was detected as monkeypox infected	[18]
4	From Nigeria to USA	July 2021	One USA citizen who traveled from Nigeria to the United States was the confirmed case of monkeypox in human	[19]
5	From Nigeria to USA	November 2021	A international traveler who traveled from Nigeria to Maryland, USA was detected afterwards as monkeypox virus infected	[20]

to be similar to the Nigeria virus strain [22]. Likewise, another monkeypox-infected case was noted in the USA, the traveler was diagnosed virus-infected, returning from an international flight from Lagos, Nigeria, to Maryland, USA [23]. Several other examples have also been demonstrated revealing cases of transmission of monkeypox virus through the air travel.

Researchers also explored the role of other modes of transport other than air travel on other epidemics, e.g., SARS, influenza A/H1N1, and Ebola. In many cases, the ships are supposed to be directly responsible for the quick spread of infectious diseases in the range of numerous animals via planned or accidental transport [24]. It also noted that highways, railways, civil aviation, subway ridership, and road transport greatly affected the spread of the disease [25,26].

Studies also found the impacts of the emergence of outbreaks of infectious diseases affect all modes/forms of transport [27]. Apart from that, the different mode of travel is also considered a potential risk route in disease emergence and spread, such as spreading insect vectors or human-incubated pathogens. These modes of travel might help to spread the pathogens a great distance in short times.

Conclusion

Though any travel link from monkeypox virus endemic countries has not been established yet to the increasing number of current monkeypox cases in non-endemic countries. Monkeypox virus is re-emerging from time to time. The root cause of the present outbreaks needs to study immediately. At the same time, the emphasis must be given to finding out the zoonotic reservoir, zoonosis, spillover of the virus from the host, etc., of this viral disease. The researchers could not find an association of monkeypox outbreaks with air traveling. However, air travel might increase the risk of spreading the disease. At the same time, continuously rising patients being seen all of a sudden in very few days that too in multiple countries requires needful extensive epidemiological investigations, genome sequencing and phylogenetic analysis of different virus isolates, to know the actual cause of the transmission and spread of this virus. With the associated travel links and zoonotic nature of the

monkeypox virus in previously reported cases and outbreaks, emphasis needs to be given to finding out the root cause of monkeypox outbreaks in different countries. The possibility should also be explored for any direct and/or indirect role of travel from any endemic country and maybe from non-endemic countries to other such countries. Furthermore, it is also necessary to understand the zoonotic event, which will help us find the natural animal reservoir(s) for the monkeypox virus that is not known until now.

Explorative research and deeper disease investigations are suggested to find out the transmission events of the recently rising cases of monkeypox virus infection in multiple non-endemic countries beyond Africa, which would help in formulating appropriate disease prevention and control measures. CDC recommended that travelers visiting Nigeria should avoid close contact with sick or monkeypox infected individuals and take appropriate measures to prevent infection by washing their hands frequently with water and soap. At the same time, it is also necessary that pregnant women, and immunocompromised travelers, who are at more risk to catch monkeypox virus infection, should keep away to travel to those areas where monkeypox outbreak is taking place. However, the medical community and aviation industry should train or educate the ordinary person regarding health issues related to air travel. They should be trained on how to prevent and control the air travel related infections. Finally, we urge every country's policymaker to formulate immediate proactive and coordinated plans and seriously to create a travel regulation to fight as per WHO guidelines [5] against monkeypox virus infection. It might aid in stopping the rapid spread of the monkeypox virus from country to country and put an end to the current episodes of monkeypox disease at the international level.

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CRediT authorship contribution statement

Manojit Bhattacharya: Validation, figure preparation. **Kuldeep Dhama:** Validation, reviewing, All authors critically reviewed and approved the final version of the manuscript. **Chiranjib Chakraborty:** Conceptualization, Data curation, Investigation, Writing – original draft, Writing – review & editing.

Declaration of competing interest

All Authors have declared no conflict of interest.

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