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Editorial

First Monkeypox deaths outside Africa: no room for complacency

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As of 16 August 2022, there are 37,632 confirmed cases of monkeypox in more than 85 non-endemic countries, plus those in endemic African areas, making a total of 38,019 in 93 countries.[1] The disease was always considered endemic in the African continent, with only a few sporadic outbreaks in the rest of the world since 2003.[2] Surprisingly, the present epidemic has wholly changed the epidemiology of the disease, with Europe and the American continent contributing more than 90% of the total confirmed cases.[3]

From the beginning of 2022 until 8 June 2022, 72 deaths were reported, all belonging to the African region. Of the total 72, the Democratic Republic of Congo (DRC) had the largest proportion with 64 deaths.[4] The disease remained confined to the African continent until the beginning of May 2022, when the first case was seen in the United Kingdom on 8 May 2022.[5] The World Health Organization (WHO) reported on 22 July 2022 that only five deaths were due to monkeypox, with all of them again from Africa.

The first death from monkeypox outside Africa was reported in Brazil on 29 July 2022, when a 41-year-old man undergoing treatment for lymphoma died of septic shock.[6] Shortly after, Europe had its first death from a monkeypox case in Spain. The identity of the deceased was not disclosed. However, according to the Spanish health authorities, the individual was a middle-aged man from Alicante (Valencia region), who died due to encephalitis.[7] Within 24 hours of the first case, Spain again confirmed its second death from monkeypox. The second case reportedly is a young man, and more details are yet to be known. Spain is the worst hit country in Europe, with more than 4,200 confirmed cases and 120 monkeypox hospitalizations.

On 31 July 2022, India reported its first monkeypox death.[8] He was a 22-year-old man who had returned from United Arab Emirates (UAE) on 21 July to Thrissur district in Kerala. Kerala is a state in the south of India that has reported the first three confirmed cases of monkeypox. He was admitted to a private hospital on 27 July 2022, with fever, encephalitis and lymph node swelling. At admission, he did not have any body rash, and therefore, there was no suspicion of monkeypox. It was only after he died that he tested positive for monkeypox at Ras Al-Khaimah (UAE) on July 19, just before his return to Kerala. According to health authorities, the deceased patient was healthy and did not have any other illness. Given the unexpected death, a high-level task force has been constituted to review the ongoing country public health preparedness.

On 1 August 2022, death due to monkeypox was also confirmed in Lima, Peru, in a 41-year-old man with HIV and tuberculosis that was not under antiretroviral treatment. He was admitted to the ICU with respiratory failure, acute renal failure and septic shock, and confirmed monkeypox virus (MPXV) infection.[9] One death has been also reported in Guayaquil, Ecuador.

Possible causes of death triggered by monkeypox infection include MPXV central nervous system (CNS) invasion with encephalitis,[10] an infrequent complication, but where cell-mediated immunity defects may play a role. Also, sepsis from a skin and soft tissue infection can complicate the associated skin lesions. During prior African

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Table 1. Comparison of CFR% among non-endemic and endemic countries during 2022, up to 16 August.

Country	Cases	Deaths	CFR%
Non-endemic countries			
India	9	1	11.11
Ecuador	17	1	5.88
Spain	5719	2	0.03
Brazil	2893	1	0.03
Subtotal non-endemic countries	37,632	5	0.01
Endemic countries			
Central African Republic	8	2	25.00
Nigeria	157	4	2.55
Ghana	47	1	2.13
Subtotal endemic countries	387	7	1.81
Total (World)	38,019	12	0.03

CFR, case fatality rate.

outbreaks – especially with the Congo basin strain – mortality was common among young children.[11] In those cases, researchers hypothesize the potential role of occasional co-infection with Varicella zoster virus (VZV). Experimental aerosolized MPXV infection among cynomolgus monkeys produced a fatal fibrinonecrotic bronchopneumonia 1–2 weeks after exposure.[12] In animal models, high MPXV viremias and neutropenias have been implicated in fatal gramme-positive sepsis.[13] Future autopsy histopathology analyses from fatal cases are needed to elucidate specific viral mechanisms of death.

Five deaths, among 37,632 cases in non-endemic countries represents, theoretically, a case fatality rate (CFR%) of 0.01%, compared with 1.81% in endemic countries during 2022 (183 times higher) (Table 1). Nevertheless, there are regional differences (Table 1). The difference would be higher when comparing with recent systematic reviews of African cases before 2022,[14] reporting 10.6% [95% confidence interval (CI), 8.4–13.3%] for clade 1 (formerly Congo basin or Central African) and 4.6% (95% CI 2.1–8.6%) for clade 2 (formerly West African). The differences may be related to multiple factors, including difference in the host (e.g. nutrition, comorbidities, immunosuppression, among others), but also to the quality of the health care systems as well as the viral evolution. In addition, transmission has primarily been between men who have sex with men (MSM), and they have generally been of a young age (20- to 40-years-old) with few comorbidities; this has changed the epidemiology and likely reduced the CFR%.

More deaths due to monkeypox are yet to come during this outbreak, especially among immunosuppressed patients. Mortality risk factors and interventions should be researched immediately to prevent, control and mitigate the disease burden.

Declarations

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Not applicable.

Consent for publication
Not applicable.

Author contributions
Ranjit Sah: Writing – original draft.

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