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Article *in* Journal of Travel Medicine · March 2021

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Journal of Travel Medicine, 2021, 1–2
doi: 10.1093/jtm/taab029
Research Letter

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The reproductive number of Lassa fever: a systematic review

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Submitted 20 January 2021; Revised 9 February 2021; Accepted 22 February 2021

Key words: Lassa fever, reproductive number, transmission, Africa

Lassa fever (LF) is an acute rodent-borne viral hemorrhagic disease, whose etiological agent is the Lassa virus (LASV). Since its first discovery in the village of Lassa, Nigeria in 1969, LF has caused endemics in West African regions including countries of the Mano River Union and Nigeria.[1] The symptoms of LF are developed approximately 21 days after infection with examples of fever, facial swelling, muscle fatigue, vomiting, cough, abnormal blood pressure and failure in multiple organs.[2] LF follows the zoonotic transmission cycle that includes animal-to-animal, animal-to-human and human-to-human transmission paths.[3] In 14 western and high-risk African countries, LASV infects from 300 000 to 500 000 individuals annually, which results in 5000 deaths, and poses risks of infection to over 37.7 million individuals.[1]

The basic reproduction number (R_0) is defined as the average number of secondary cases generated by a primary case during its infectious period in a completely susceptible population, which is commonly adopted to characterize the potential to cause an epidemic of an infectious disease.[4] When R_0 is less than 1, the epidemic curve is expected to decline with the decreased number of new cases, and *vice versa*.

We conducted a systematic review on the value of R_0 of LF that covered published peer-reviewed literature from 1969 to 2020. Following the 'Preferred Reporting Items for Systematic reviews and Meta-Analyses' (PRISMA) guideline,[5] we searched MEDLINE, Embase and PubMed without language restriction. Relevant references were also searched by reviewing the reference list of the included articles. The detailed searching and screening strategies and outcomes are presented in Supplementary Information. We identified 173 articles in total, among which 80 were from Embase, 42 were from MEDLINE, 50 were from PubMed and 0 articles were identified from other sources. There were 98 studies left after removing the duplicates. After 65 articles were excluded after the title or abstract screening, we retrieved 33 articles eligible for the full-text assessment. We excluded 21 articles because of irrelevant topics, lack of data or ineligible article types. Eventually, we selected five studies that analyzed eight separated LF epidemics, and we included them in this review.

The R_0 estimates are summarized in Table 1 with different areas of LF outbreaks, study periods, types of model and transmission paths. There were four out of the five selected studies that investigated the LF outbreaks in Nigeria, which is one of the places where LF appears prevalent annually. The R_0 estimates are larger than 1 in the five selected studies, which range from 1.1 to 1.8 for human-to-human transmission and from 1.5 to 1.7 for rodent-to-rodent transmission. As opposed to other types of febrile diseases (such as yellow fever and dengue), little variations in the R_0 of LF were noted among different places, regional settings, study periods or methodological differences.

Table 1. Published estimates of R_0 for Lassa fever

Study	Area(s) of LF outbreaks	Study period	R_0 estimates	Type of model	Transmission path
Akhmetzhanov *et al*.[7]	Nigeria	wk 4, 2016—wk 30, 2018	1.74	Compartmental model	Human-to-human
Iacono *et al*.[8]	Jos, Nigeria and Zorzor, Liberia	1970 and 1972	1.68	Exponential growth model	Human-to-human
Musa *et al*.[9]	Nigeria	2016—2019	1.84	Sub-exponential growth model	Human-to-human
Zhao *et al*.[3]	Nigeria	Nov 2016—May 2017 Nov 2017—May 2018 Nov 2018—Mar 2019	1.23 (95%CI 1.22—1.24) 1.33 (95%CI 1.29—1.37) range: 1.08—1.36	Sigmoid growth model	Human-to-human
Nuismer *et al*.[10]	Bantou, Guinea Tanganya, Guinea	2002—2005 2002—2005	1.74 1.54	Compartmental model	Rodent-to-rodent

As a zoonosis, LASV spreads from rodents to humans, yet so far, we find no evidence of the scale of R_0 for rodent-to-human transmission.

To date, there is a lack of vaccine for humans against LASV. As such, it appears challenging to prevent the transmission of LASV, especially among countries with less developed or poor healthcare settings. The LF control measures are of public health importance in mitigating the outbreaks. These control measures include reducing the abundance of rodents, sterilizing and to avoid exposure to the contaminated food or household items and maintaining personal hygiene, especially during the rainy season. Given the urgency of regional LF endemics, scientists in the Institut Pasteur identified one of the vaccine candidates, and the development of this vaccine entered a stage of human clinical trials since 2019,[6] which brings hopes to fight against LF. We approximated the vaccine threshold using the formula of $(1-1/R_0)\times 100\%$.[4] Given R_0 ranging from 1.1 to 1.8, the herd immunity threshold, i.e. the proportion of the population to be vaccinated, ranges from 9 to 44%, if an ideal 100% vaccine protective ratio is assumed. This proportion increases to a range of 18 and 88% when the vaccine protective ratio reduces at 50%. We remark that a vaccine coverage around 50% may be logistically feasible in the current settings of western African regions, where LF is endemic.

We conclude that although the evidence suggests R_0 of LF does not vary in different settings, the vaccine coverage thresholds vary substantially depending on the LASV transmissibility and vaccine protective ratio. In the current situation without an available vaccine, the control measures are critically important to mitigate LF epidemics.

Supplementary data

Supplementary data are available at *JTM* online.

Acknowledgements

None.

Authors' contributions

J. Wang and S. Zhao conceived the study. All authors conducted literature search, collected the data, carried out the analysis, drafted the manuscript, discussed the results, revised the manuscript and gave final approval for publication.

Funding

The authors received no specific funding for this work.

Conflict of interests

The authors declared no conflict of interest.

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