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LETTERS TO THE EDITOR

Addressing the Lassa Fever Epidemic in West Africa: A Mathematical Modelling Approach

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Abstract

Lassa fever is a viral haemorraghic fever, accounting for about 5,000-10,000 deaths annually. The disease is endemic in West-Africa with seasonal epidemics. We proposed that with the use of mathematical modelling studies, we can predict accurately when the outbreak will likely occur by computing the infectivity rate, weather patterns and population of rodents. With this, adequate preventive measures and public health control interventions can be put in place to prevent the outbreak. This necessitates the need for more policy-relevant mathematical modelling studies on Lassa Fever, starting with building capacity in sub-Saharan Africa, where the disease is prevalent.

Keywords: Lassa fever, mathematical modelling, West Africa, *Mastomys*

Lassa Fever is an acute viral haemorrhagic illness caused by Lassa virus, primarily transmitted to humans via contact with household items contaminated with urine or faeces from multimammate Mastomys rat (1). It is also transmitted via human-to-human transmission from direct contact with the blood, secretions, or other body fluid of infected persons, especially in health care settings (2). While it was originally discovered in Nigeria, it is endemic in many West African countries, such as Benin, Ghana, Sierra Leone, Liberia, Mali, and Guinea (3). Nonetheless, sporadic cases have been seen in travelers returning to Holland, Germany, and the United Kingdom (4). As recent as February 2022, the United Kingdom confirmed two laboratory and one probable cases of Lassa fever (5), indicating that it is a disease of public health importance with pandemic potential. There are usually about 100,000-300,000 infections annually with approximately 5,000-10,000 deaths (6). As of week 25 of 2022, about 5,495 suspected cases have been recorded in Nigeria, with 820 confirmed cases and 160 deaths— a case fatality ratio of about 19.4% (7).

The incubation period of Lassa fever ranges from 6–21 days, with deaths usually occurring within 14 days of onset in fatal cases. It is especially severe late in pregnancy, with maternal death and/or fetal loss occurring in more than 80% of cases during the third trimester (1). Convincingly, the most critical issue with Lassa fever control is clinical misdiagnosis of the disease. This stems from the non-classical presentation of the disease, as the initial symptoms—malaise, fever, fatigue, headache—often mimic those of other West African endemic diseases, such as malaria and typhoid fever. Also due to the absence of a rapid diagnostic test, the disease is often missed at the early stage and diagnosis is made when it is already advanced. This also makes health workers particularly vulnerable to the disease, as Nigeria alone has lost over 71 health workers to the disease since its discovery (8), further straining the already overwhelmed health workforce. And while Ribavirin, the non-licensed drug for treating the virus, has shown promising effects, it is majorly effective when used during the early incubation period—first seven days of infection (9). Thus, there is a need for high degree of suspicion to avert mortality secondary to the disease.

Considering Lassa fever epidemic is seasonal, usually in the dry season following the reproductive cycle of Mastomys spp. in rainy season (10), an innovative tool such as computational and mathematical modelling can help in predicting the accurate time and place to expect the outbreak, thereby allowing the necessary preventive and control measures to be put in place to prevent the outbreak. Unfortunately, despite the inclusion of Lassa Fever in the Blueprint list of priority diseases for research and development by the WHO in 2018 (11), only few mathematical modelling studies have been conducted on the disease compared to other infectious diseases (10). Ibrahim and Denes (12) established and researched a compartmental epidemic model of Lassa

Fever transmission dynamics, showing that while human-human transmission has significant effects on the disease prevalence, the most relevant factors in Lassa's periodicity are rodent-related variables. Zhao et al. (13) utilized different mathematical models to analyze the epidemiological characteristics of Lassa fever epidemics in different areas in Nigeria and quantify the relationship between the basic reproduction number and state rainfall. Another study conducted by Akhmetzhanov et al. (14) analyzed the seasonal drivers of Lassa fever epidemics in Nigeria through mathematical models, which analyzed the datasets of human infection, rodent population, and climate change. Although these studies provide insights into different factors at play in Lassa fever transmission dynamics, no comprehensive mathematical modelling study has accurately predicted "where" and "when" to expect an outbreak, thereby limiting the use of these studies to inform public health decisions (15). Perhaps, this might have stemmed from the relatively weak disease surveillance system in West Africa, resulting in unavailability of epidemiologically relevant data, such as the population of rodents, changes in weather patterns, infectivity rate and other relevant factors that can be computed to design an accurate predictive model for Lassa fever transmission during different seasons (15,16). This calls for the need to increase epidemiological surveillance in this region to accurately measure these factors to provide real-time, quality data for mathematical modellers to utilize. If this could be done, the public health response to Lassa fever control is likely to be more effective. For instance, timely advocacy on the disease will ensure health workers are proactive with the use of Personal Protective Equipment (PPE) and also have a high degree of suspicion for the disease, thereby sending samples for laboratory diagnosis, administering ribavirin and isolating suspected cases on time. Likewise, advocating to the populace will ensure good "community hygiene" practices, consequently preventing Mastomys rodents from entering homes. Thus, mathematical modelling is a highly effective policy tool in mitigating the burden of Lassa fever in West Africa and eradicating the disease. Furthermore, with the identification of potential vaccine candidates for Lassa Fever—still in the clinical trial phase—mathematical models can predict the cost-benefits and cost-effectiveness of introducing the vaccine and the best strategy to roll out the vaccine to achieve maximum impact, thereby serving as an advocacy tool to policymakers.

However, there is a lack of capacity in mathematical modelling of infectious diseases in sub-Saharan Africa. Adetokunboh et al. (17) posited that while research output in applied epidemiological modelling of infectious diseases studies might have increased in sub-Saharan Africa, there is still an under-representation of African researchers as leading authors. Hence, in order to mitigate the burden of Lassa fever and other endemic diseases of public health importance in sub-Saharan Africa (sSA), it is germane to increase the pool of infectious disease modellers in the region. Not only this, it is crucial that these potential modellers collaborate with relevant agencies, such as countries' Centres for Disease Control (CDC) and Ministries of Health, to conduct policy-relevant research, whose findings can be utilized to inform public health decisions, and not only for academic purposes. As a step in the right direction, in 2021, the Bill and Melinda Gates Foundation (BMGF) sent out a request for proposal of 1 million USD worth to strengthen the malaria mathematical modelling ecosystem in sSA by increasing the number of PhD-trained mathematical modellers in sSA, bringing together different modelling units across sSA to share expertise and improving modellers' access to timely, high-quality data (18). This investment has the potential to amplify mathematical modelling studies on sub-Saharan African endemic diseases, including Lassa Fever. However, to ensure sustainability, it is pertinent for the governments of this region and all relevant stakeholders, such as donors, R&D partners and local academic institutions, to prioritize investing in this area.

Competing Interests
There are no relevant financial or non-financial competing interests to report.

Authors' Contributions

Sodiq Inaolaji Yusuff: Conceptualizing the topic; conducting literature review; and writing the manuscript

Iyiola Olatunji Oladunjoye: Conceptualizing the topic, writing the manuscript, and finding the right journal

Olalekan Tolulope Popoola: Drafting the recommendation and reviewing the manuscript

Kunle Oreagba: Conceptualizing the topic and revising the manuscript

Bolarinwa Olufunmilayo Victoria: Conducting literature review, writing some sections of the article and revising the manuscript

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