Main

Nowadays the scientific community has become quite cognizant of the effects of climate change on disease outbreaks across the world. The effects of adverse climate and weather events on spread of vector borne diseases has been well documented 1–3. For example, 58% of human infectious diseases are estimated to have increased risk of spread that can be attributed to climate change 4. Increasingly, neglected tropical diseases which were historically localized to certain endemic zones have now been reported to have incidences in neighboring previously unaffected areas. Carlson et al. (2022), estimated that globally more than 3000 mammalian species, including rodents, are expected to change habitats by 2070 5. Paradoxically, the regions expected to be most affected by these tumultuous changes in disease risk are those which contributed the lowest, historically, to climate burdens 6.

Tropical and sub-tropical countries in the continents of Africa, Asia and South America have been disproportionately affected by the increased risk of neglected disease outbreaks that are severely perturbed by climate change events. Surface temperature in South American countries, in particular, is expected to rise between 0.92 to 6.14 °C depending on the Shared Socio-economic Pathways (SSP) model of CMIP6 by the end of 21st century 7. Similarly, the precipitation interspersed with long droughts and high chances of wildfires might become a common occurrence in the forested and grass regions of South American continent.

Similar to insect and invertebrate vector-borne diseases, we can reasonably expect there to be profound effects of climate change on disease dynamics of rodent-borne diseases 1,2,8. For example, the hotspots for spillover of Lassa Fever in Western African countries are forecasted to increase as the regional climate changes over the next few decades 9. Similarly, several studies reviewed by Guterres and de Lemos (2018) demonstrated that zoonotic outbreaks of rodent-borne hantaviral infections can be predicted with reasonable accuracy using environmental and climatic features 10. Given the expected changes in the climatic conditions in the global south, we theorized that rodent-borne infections which are heavily dependent on the eco-habitat of rodent reservoirs would spread to previously incidence-less or sparsely incident areas.

Particularly, the risk of mammarenaviral infections to humans, such as Lassa Fever or Argentine hemorrhagic fever, which are some of the deadliest of zoonotic hemorrhagic fevers will be perturbed given the expected changes in climate and environment in the coming 2-5 decades. Zoonotic arenavirus spillover into humans is heavily dependent on the distribution patterns of their wild rodent reservoirs, the contact between humans and these rodents due anthropogenic activities like deforestation, human movements, changing agricultural patterns, etc. and the increasing domestic/ peri-domestic behavior of these rodents through human habitats 11. The main routes of transmission include fomites, dried droppings and urine through the oral route and less frequently through breathing, scratches and bites from the reservoir host through non-oral routes 12,13. Recently, more zoonotic arenaviruses that are emerging have been reported. For example, in Asia, Blasdell et al. (2016) reported two novel arenaviruses with zoonotic potential in Cambodia, Thailand, and Laos 14. Additionally, we estimated that ecological habitats of the rodent reservoirs of the known zoonotic arenaviruses such as *Calomys musculinus* of Junin virus (which causes Argentine Hemorrhagic Fever; AHF) will change radically in the future as a direct response to changing climate 15.

In the case of South America, the New World Arenaviruses (NWA) such as Guanarito virus in Venezuela and Columbia, Machupo virus in Bolivia and Paraguay and Junin Virus in Argentina have had multiple human outbreaks that caused mortality between 5% to 30% 16. As mentioned previously, we could reasonably expect drastic changes to the habitats of the rodent reservoirs of these zoonotic arenaviruses due to changes in food availability, climatic events, changes in human population dynamics and increasing collisions with wild rodents in South America, all of which could be attributed to be affected by climate change to some degree.

While Old World Arenaviruses (OWA) such as Lassa Fever virus in Africa have been modeled and studied extensively from the perspective of disease dynamics and transmission risk 17, until now, to our knowledge, none of the NWAs had been modeled to that extent. Moreover, the impact of climate change on the disease dynamics of both OWA and NWA had not been established yet. However, the disease dynamics of these rodent-borne zoonotic NWAs and their sensitivity to climate change posed a complex modeling challenge and was not straightforward. Conditions necessary for zoonotic spillover depend on the direct and the indirect interaction of susceptible humans and infectious rodents. To quantify the changing risks, the ecology of the rodent reservoirs needed to be considered in tandem with the human population and expected changes within these aspects due to climate change. Modeling frameworks such as Species Distribution Models (SDMs) which can incorporate bioclimatic and environmental factors for estimating the habitats of the rodent reservoirs could be effectively employed in such cases 18. Since the model signals for association of climate change with species distribution were not expected to be monotonic but rather complex and subtle, modifying SDM framework to employ ensemble tree based techniques such as Random Forest (RF), Extra Trees (ET), eXtra Gradient Boost (XGB) and Light Gradient Boost Models (LGBM) seemed warranted 19.

The aim of this study was to determine the impact of climate change on the risk of New World Arenavirus (NWA) outbreaks in South America. To achieve this aim, we planned to develop a modeling framework that involved incorporating Species Distribution Models (SDMs) of rodent reservoirs of NWAs using bioclimatic and environmental geo-spatial data with mechanistic Force-of-Infection (FOI) model on human population data in the same geo-spatial regions. We planned to apply this modeling framework to six identified rodent reservoirs of the three most reported NWAs, namely, Guanarito virus, Machupo virus and Junin virus. We also aimed to predict the projected species distribution patterns of the rodent reservoirs in the future (2041-2060) and likewise the FOI patterns for human outbreak risk using the climate change scenarios under Shared Socio-economic Pathways (SSP scenarios) of Coupled Model Intercomparison Project Phase 6 (CMIP6) of IPCC 20. Finally, we aimed to gain insight in the association between projected changes in the bioclimatic and environmental data and the projected changes in the FOI. Here, we presented the transmission risk derived from the FOI by identifying the potential hotspots for zoonotic outbreaks of NWA currently and in the future.

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