

Modelling of epidemic cycles of visceral leishmaniasis in the Indian subcontinent

Supervisors: Drs L. Chapman & D. Hollingsworth, (both WIDER group). Reserved for T. Pollington

Abstract

An epidemiological dataset of visceral leishmaniasis (VL) will be spatially analysed. Parsimonious models involving established transmission factors, migration and regional differences will be used to try to describe the reported epidemic cycles of VL. VL has been modelled relatively little and the use of stochastic individual-based models (IBMs) with spatial structure and seasonal migration in this project is original.

Research context and modelling considerations

Visceral leishmaniasis is a neglected tropical disease targeted by WHO for elimination as a public health problem (<1 case/10K people/year) from the Indian subcontinent by the end of the decade—based on strong intergovernmental commitment, better diagnostic tools, enhanced surveillance, scaling-up sandfly control and faster access to medicines [1]. Falling reported cases in Bihar (India) from 25,222 to 7,615 (2011-2014) support this strategy [2], yet under-reporting, presence of asymptomatics [3] and recurring epidemic cycles present major hurdles to elimination.. This project will use an epidemiological dataset from a community study of VL cases from 5118 households in rural villages in Bangladesh between 2007 and 2010 [4]. It will spatially analyse disease progression within households and across the villages. Understanding these dynamics at a village level may help explain the 10-15 year epidemic cycles seen regionally. Published state-to-state commuter movements can provide seasonal human migration parameters for parameterisation of an IBM. No IBMs have yet been developed for VL [5]. Regional asynchronicity of epidemics and differentiated protective immunity could drive VL recurrence events. Developing metapopulation models with sufficiently simple structures that can produce these effects could help to explain the epidemic cycles of VL. Since epidemic cycles may have existed for centuries, the hypothesis is that parsimonious models, which do not account for modern vector control and chemotherapy activities, are still capable of reproducing this cyclical behaviour.

The data

Prof C. Bern (UCSF, USA) administered the epidemiological study, cleaned the data and now kindly provides it to us. Despite analysis of an earlier subset mainly involving VL cases, this later dataset covers post kala-azar dermal leishmaniasis cases also—a potential sequela of VL recovery. The pseudo-anonymised data contains patient histories and geolocations so we will use encrypted local drive or university network drives. Ethics and informed consent has already been obtained [4].

Avenues for PhD research

- > Time-series spectral analysis of longitudinal data from Indian archives.
- > Incorporating village-level dynamics with transmission at the sub-district level (CARE India data)
- > Effect of *L. donovani* strains[6], their competition or cooperation and implications for R_0 estimates.
- > How VL can persist at low endemic levels, invisible from current surveillance, at the detection threshold and yet re-appear as periodic cycles; quantify the necessary quality of diagnostics (patient-level) and case detection (regional-level) to make the disease sufficiently visible.
- > Quantify the importance of unknown/uncertain parameters through sensitivity analyses on popular models. Use this to direct the research community on which measurements should be collected in future epidemiological studies.

References

- [1] Accelerating work to overcome the global impact of neglected tropical diseases – a roadmap for intervention. WHO 2012. who.int/neglected_diseases/NTD_RoadMap_2012_Fullversion.pdf
- [2] India makes good progress in combating kala-azar. *The Lancet*. Vol 385 May 2, 2015
[thelancet.com/pdfs/journals/lancet/PIIS0140-6736\(15\)60877-7.pdf](http://thelancet.com/pdfs/journals/lancet/PIIS0140-6736(15)60877-7.pdf)
- [3] Asymptomatic *Leishmania* infections in northern India: a threat for the elimination programme? *Trans R Soc Trop Med Hyg.* 2014 Nov;108(11):679-84.
- [4] Islam *et al.* Clinical and Immunological Aspects of Post–Kala-Azar Dermal Leishmaniasis in Bangladesh. *Am. J. Trop. Med. Hyg.*, 89(2), 2013, pp. 345–353
- [5] Rock K *et al.* Uniting mathematics and biology for control of visceral leishmaniasis. *Trends in Parasitology* June 2015, Vol. 31, No. 6 <http://dx.doi.org/10.1016/j.pt.2015.03.007>
- [6] Srivastava *et al.* Genetic Heterogeneity in Clinical Isolates of *Leishmania donovani* from India. *J Clin Microbiol.* 2011 Oct; 49(10): 3687–3690.