

Drivers of Typhoid Fever Transmission in Kathmandu, Nepal: A Mathematical Modelling Study

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Background: A substantial proportion of the typhoid fever burden occurs in South Asia. Kathmandu, Nepal experienced a marked increase in the number of diagnosed *Salmonella enterica* serovar Typhi cases between 2000 and 2003, which subsequently declined but to a higher endemic level than in 2000. This epidemic of *S. Typhi* coincided with the increased occurrence of multi-drug resistant typhoid and, in particular, the emergence of the *S. Typhi* H58 haplotype, but might also have been fuelled by the highly migratory population in Nepal.

Methods: We used a mathematical modelling approach to investigate potential epidemic drivers and fit our mathematical model to weekly data on *S. Typhi* cases between April 1997 to June 2011 and to the age distribution of *S. Typhi* cases. We explored whether the epidemic of typhoid fever in Nepal was driven by (1) heightened levels of migration, (2) the emergence of multi-drug resistant typhoid or (3) a combination of both increased migration and rise in multi-drug resistant typhoid.

Results: Models allowing for the migration of susceptible individuals, alone or in combination with the emergence of multi-drug resistance, provided a good fit to the data. The emergence of multi-drug resistant typhoid alone, either through an increase in disease duration or the transmission rate, could not fully explain the pattern of *S. Typhi* cases.

Conclusions: Our analysis suggests that the epidemics were caused by the migration of susceptible individuals to the capital and possibly aided by the emergence of multi-drug resistant typhoid. This underlines the importance of identifying and targeting migrant populations to prevent disease transmission and infection.