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Perspective

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Traveller studies in low- and middle-income countries: a critical gap in global antibiotic resistance surveillance

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Background

Antibiotic resistance (AR) is a global public health threat. Antibiotic use is the primary driver of AR; however, once AR genes (ARGs) have been mobilized by pathogenic or commensal bacteria, they can propagate among bacterial communities harboured by humans and animals even in the absence of strong selective pressures. Global trade and travel have drastically increased human interactions across diverse environments and ecosystems and are known to facilitate the spread of antibiotic-resistant bacteria and ARGs. Since the 1990s, studies that screen travellers' gut microbiomes pre- and post-travel, i.e. 'traveller studies', have identified world regions where the risk of acquiring AR is especially high, as well as which ARG alleles and resistance-conferring point mutations predominate in those regions.[1] In this way, traveller studies have proved to be a cost-effective approach for global AR surveillance.

To date, almost all traveller studies have surveyed individuals travelling from high-income Western countries (primarily in Europe) to low- and middle-income countries (LMICs) in the global South.[1] While these studies have identified 'sources' of AR to high-income countries, the opportunity to use traveller studies to understand the dissemination of AR and ARGs among LMICs themselves has not been leveraged. This is a clear gap given that a substantial proportion of global travel occurs between LMICs, especially for the purposes of migration, medical tourism, trade and employment, and this is likely to accelerate due to climate-change-related migration.[2] Currently, 70–80% of migrants relocate to countries in the same world region.[2] According to the United Nations High Commissioner for Refugees' annual Global Trends report, the number of refugees stands at 22.5 million (~55% from Syria, Afghanistan and South Sudan), and LMICs have provided asylum to 28% of this total.[3] Separate from emigration, approximately five of every 1000 travellers come into contact with healthcare systems while abroad[4] and globally, most medical travel is intra-regional in nature.[5] In 2008, Indonesians, for example, comprised nearly three-quarters of all recorded medical travellers to Malaysia.[5] Recently, the US CDC has supported a concerted effort to begin identifying drivers for AR acquisition in LMIC community settings, recognizing the impact that AR has on global health and security.[6] In this commentary, we highlight the need to better understand travel patterns of individuals between LMICs to better inform public health strategies to curb the global spread of AR.

Potential policy implications of traveller studies based in LMICs

Understanding the dynamics of AR spread between LMICs could significantly shape policy at several levels. In medical systems, healthcare providers could make more informed empirical treatment decisions based on a patient's travel history and seek additional screening for high-risk patients. At a country level, public health systems could begin to identify AR patterns unique to certain countries and potentially document practices (e.g. lack of wastewater collection and treatment) driving the development and spread of these strains. At the global level, traveller studies between LMICs could help the global health community tailor intervention strategies for countries where AR in their communities is largely driven by trade, importation or workforce movement from another country. Given that many LMICs lack the resources needed to routinely survey humans, animals and the environment for AR, the putative benefits of traveller studies based in LMICs are arguably higher with regards to global AR surveillance.

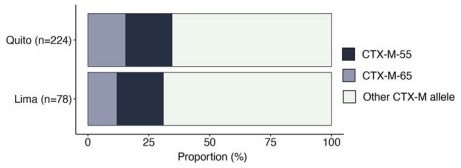

Figure 1 Distribution of *bla*$_{\text{CTX-M}}$ alleles among *Escherichia coli* isolated from children in Lima, Peru (2016–2018) and children, dogs and chickens in Quito, Ecuador (2018). Data adapted from Salinas *et al.*, 2021 (doi: 10.1289/EHP7729) and Nadimpalli *et al.*, 2024 (doi: 10.1080/19490976.2024.2309681)

Case study: tracking the origins of *bla*$_{\text{CTX-M-55}}$ and *bla*$_{\text{CTX-M-65}}$ to Peru and Ecuador

We recently noted the potential value of inter-LMIC traveller studies when trying to untangle the potential source of *bla*$_{\text{CTX-M-55}}$ and *bla*$_{\text{CTX-M-65}}$ genes to Peru and Ecuador. Enterobacterales that harbour extended-spectrum beta lactamase (ESBL) genes, like *bla*$_{\text{CTX-M}}$ alleles, are considered a 'critical threat' to human health by the US CDC. Multiple traveller studies have examined risk factors for their acquisition among travellers from high-income settings to the Global South.[1]

US studies have identified Andean countries as sources of *bla*$_{\text{CTX-M-65}}$ to sick travellers and potentially to US poultry.[7] In our recently published work, we noted that ESBL-producing *Escherichia coli* detected in Peru and Ecuador frequently harboured the *bla*$_{\text{CTX-M-55}}$ and *bla*$_{\text{CTX-M-65}}$ alleles (Figure 1). This finding is unusual because while neither of these alleles predominate in either the US or Europe, they are exceptionally common in East and Southeast Asia. Other studies reporting *bla*$_{\text{CTX-M-55}}$ and *bla*$_{\text{CTX-M-65}}$ in the Andean region have hypothesized that they may have been 'imported' from China through human mobilization or trade, which has sharply increased between these world regions over the past two decades. For both Peru and Ecuador, China is now a top import and export partner country and is a major investor in the region's energy, infrastructure and mining industries.[8] Importantly, as is the case in many countries benefiting from China's 'Belt and Road Initiative', this investment has been paralleled by major increases in migrant Chinese workers who staff state-funded infrastructure projects, sometimes comprising up to 40% of a project's workforce (according to local media sources).[9] In 2014, over 7000 temporary migrant Chinese workers were known to be in Ecuador for Chinese-owned projects, accounting for nearly one-third of all Chinese workers in Latin America.[10] While China largely imports agricultural products and raw materials from Latin American countries, it primarily exports technology, expertise and support services for state-owned infrastructure projects,[10] suggesting that human mobilization associated with Chinese-owned infrastructure projects could be the underlying cause for shared *bla*$_{\text{CTX}}$ gene epidemiology between these two world regions.

Elucidating this is challenging, however, given major gaps in *bla*$_{\text{CTM-M}}$ surveillance in Andean countries over time. Most studies of *bla*$_{\text{CTX-M-55}}$ and *bla*$_{\text{CTX-M-65}}$-producing bacteria have been conducted in Asia, where both alleles were first identified around 2007. In South American countries, neither *bla*$_{\text{CTX-M-55}}$ nor *bla*$_{\text{CTX-M-65}}$ were reported to predominate among ESBL-producing bacteria from humans, animals or the environment until after 2015; however relatively few studies have investigated ESBL allele distributions in this world region. Two studies in Brazil[11] and Bolivia[12] have examined the genetic contexts of *bla*$_{\text{CTX-M-55}}$ and *bla*$_{\text{CTX-M-65}}$ and noted that plasmids harbouring these alleles (IncI1, IncFII/N-ST1, IncFII, IncF33:A-:B) have previously been reported in Asian settings, suggesting potential directionality of transmission. However, given the stated gaps in primary data collection, it is difficult to draw robust conclusions about the potential origin of these alleles to the Andean region.

Conclusion

Interconnectivity between LMICs has multiple benefits for individuals, including access to labour markets, medical care and personal safety from social unrest in their home country, but this movement of individuals increases the spread of AR, potentially augmenting treatment failures across borders. Recent studies have demonstrated that travellers are effective sentinels for identifying AR reservoirs and prevalence in countries that do not have a robust surveillance framework. We propose that public health institutions based in the global North should build upon recent research efforts in LMICs to set priorities for inter-LMIC traveller studies.[6] We note that more diverse types of expertise will need to be included in these efforts—demographers, sociologists, climate scientists, economists, for example—to help the infectious disease community understand the environmental, economic, social and political relationships that are the fundamental determinants of AR spread.

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Author contributions

Jay Graham (Conceptualization-Equal, Data curation-Supporting, Project administration-Equal, Supervision-Equal, Visualization-Supporting, Writing—original draft-Equal, Writing—review & editing-Equal), Nam Nguyen (Data curation-Lead, Formal analysis-Supporting, Writing—review & editing-Supporting), Dania Hussain (Data curation-Supporting, Formal analysis-Supporting, Writing—review & editing-Equal), Maya Nadimpalli (Conceptualization-Equal, Data curation-Supporting, Formal analysis-Supporting, Project administration-Equal, Supervision-Equal, Visualization-Lead, Writing—original draft-Equal, Writing—review & editing-Equal).

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