




Review

An opportunity for global antimicrobial stewardship research: Refugee populations

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Abstract

Antimicrobial resistance is a well-known global health threat that has higher prevalence in the refugee population. Although guidance has been provided by the World Health Organization and Centers for Disease Control and Prevention on implementing antimicrobial stewardship in lower- and middle-income countries, as well as by the United Nations Refugee Agency on other infection prevention and control efforts, no specific guidance exists for implementation of stewardship in this population. We highlight challenges specific to this population, review recent studies of interest within this space, and propose a research agenda to help move stewardship forward in the refugee population. We advocate for the importance of this issue, particularly given recent current events of geopolitical volatility that render this population more vulnerable, in the setting of its already well-known numerous health challenges.

Keywords: antimicrobial stewardship; refugees; infection control and prevention; global health; public health; multidrug-resistant organisms

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Antimicrobial resistance (AMR) is a well-known global health threat that has been documented with higher prevalence within the refugee population in numerous observational and cohort studies. Such studies have mostly been performed or led by authors from high-income countries.^{1–5} Antimicrobial stewardship programs (ASPs), one of the cornerstones of the Global Action Plan on AMR outlined by the World Health Organization (WHO), have been well studied in resource-rich and resource-limited countries but are less described in refugee populations.^{6–10}

Burden, barriers, and gaps

Although reviews of AMR within refugees have broadly recommended focused screening and use of transmission-based precautions, little else has been detailed on best practices for infection control and prevention within this population, and even less has been considered regarding ASP implementation. Unique challenges exist for ASP implementation within lower- and middle-income countries (LMICs), including political instability, lack of specific governance policies and guidelines, inadequate funding and infrastructure, limited diagnostic and surveillance systems including microbiology laboratories, limited antimicrobial access, inadequate water, sanitation and hygiene (WASH) measures, lack

of qualified personnel and training programs, and high infectious disease burden.^{6,9,11,12} Furthermore, there is a high prevalence of inappropriate antimicrobial use in LMICs for numerous reasons including inadequate education on appropriate use of such agents, easier access to these agents from pharmacies and social contacts as opposed to primary healthcare facilities, and lack of enforced regulations on antimicrobial use, among others.¹³ These barriers are most likely applicable to refugee settings because most of this population worldwide resides in LMICs.¹⁴ The effectiveness of many interventions within LMICs has also been difficult to evaluate due to differences in intervention and outcome evaluations, underinvestment in surveillance capacity, as well as limited quality of related studies.¹⁰ The WHO and Centers for Disease Control and Prevention (CDC) have published guidelines to assist with ASP development in LMICs, but no specific guidance has been issued on special considerations for refugees.^{15,16} Indeed, there remains lack of guidelines or a common framework from organizations such as the WHO and Médecins Sans Frontières (MSF) and very limited data overall on general medical care of refugees, who reside in settings ranging from self-settled camps to collective centers^{17–19} and who face an infectious disease burden that varies widely with migrant group, ranging from tuberculosis to measles to parasitic infections.^{20–22} We summarize existing knowledge gaps, associated challenges, and suggested solutions in Table 1. This population requires attention for the global antimicrobial stewardship research agenda, given these many health challenges described above, such as intractable substandard living conditions, persistent overcrowding, and malnutrition, among others, that render refugees more prone and vulnerable to infection.²³

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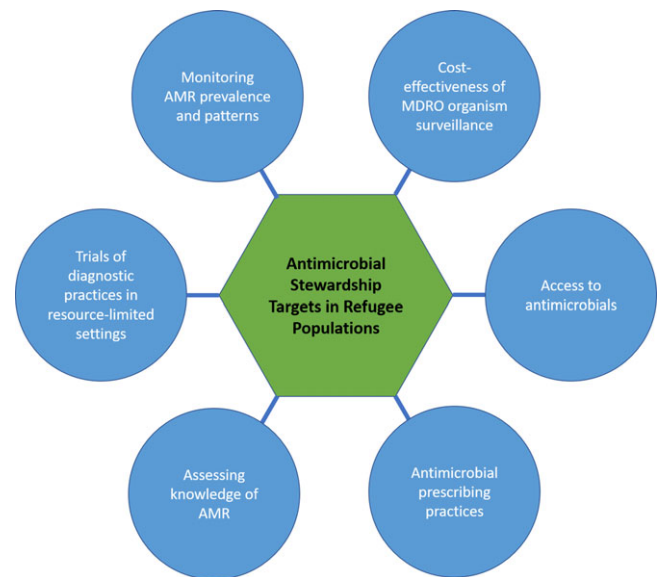
Table 1. Knowledge Gaps, Associated Challenges, and Proposed Solutions in Antimicrobial Stewardship and Overall Infection Control and Prevention in Refugee Populations

Gaps	Challenges	Solutions
<ul style="list-style-type: none"> • Lack of guidelines or common framework on general care of refugees from countries as well as institutions such as WHO and MSF • Little detail on best practices for infection control and prevention in refugee populations • No specific guidance on antimicrobial stewardship in refugee populations 	<ul style="list-style-type: none"> • Political instability • Lack of specific governance policies and guidelines with respect to refugees • Inadequate funding and infrastructure • Limited diagnostic and surveillance systems for microbiology • Limited antimicrobial access • Inadequate WASH measures • Lack of qualified personnel and training programs • High infectious disease burden • High prevalence of inappropriate antimicrobial use 	<ul style="list-style-type: none"> • Increased research efforts to inform ASP implementation in refugee population • Strengthening of already existing IPC, WASH, and antimicrobial stewardship efforts, particularly in LMICs • Application of lessons learned from IPC and WASH to guide agenda setting in antimicrobial stewardship research • Advocacy of publication of and adherence to guidelines for ASP at institutional and national level

Note. WHO, World Health Organization; MSF, Médecins Sans Frontières; ASP, antimicrobial stewardship program; WASH, water, sanitation and hygiene; IPC, infection control and prevention; LMICs, lower- and middle-income countries.

Existing evidence

Existing studies of the refugee population highlight useful information for ASP development in their respective regions and could be used to direct a framework for research on this issue. A cross-sectional study in a rural district in Uganda that hosts refugees from South Sudan and the Democratic Republic of Congo evaluated antibiotic prescribing practices, finding numerous instances of noncompliance with national guidelines, including prescriptions for conditions without any indication for antibiotics such as malaria, viral infection, and noninfectious entities like dysmenorrhea.²⁴ The study suggested several potential root causes, such as inadequate training and lack of diagnostic capacity.²⁴ Another study at the Thailand-Myanmar border found that in a population largely comprised of migrants and refugees, combined point-of-care testing of urinary tract infections (urine dipstick and microscopy together) improved appropriate antimicrobial prescribing, showing the use of only one test (urine dipstick or urine microscopy alone versus both tests combined when compared to urine culture as the gold standard) to be ineffective in the setting of high prevalence of multidrug resistance in the area.²⁵ A qualitative, cross-sectional study in which Palestinian refugees at Jordanian refugee camps were interviewed revealed high prevalence of inappropriate antibiotic use, poor knowledge base of antibiotic side effects and resistance, and long wait times to see providers, preventing refugees from seeking medical advice.²⁶ Most inappropriate use was attributed to over-the-counter acquisition of antibiotics without a prescription and self-medication at home or the use of leftover antibiotics from social contacts.²⁶ A survey via interview and chart review of pediatric patients within the Rohingya refugee population receiving care at free monthly clinics showed that nearly three-quarters of antimicrobials were not appropriately prescribed.²⁷ The majority of this was due to lack of documented diagnosis for antibiotic indication due to lack of time or lack of availability of the indicated antibiotic resulting in prescription of a different agent.²⁷ Like much of antimicrobial stewardship, local characteristics will influence ASP outcomes and implementation, but regional studies of refugee populations could be impactful.

**Fig. 1.** Proposed lines of inquiry in antimicrobial stewardship in refugee populations.

Research need

Although it is just a tiny fraction of the published literature on refugee health, the existing studies on antibiotic use in this population lay groundwork for future research to inform ASP implementation in this population. In Figure 1, we describe potential fields of inquiry including monitoring of AMR prevalence and patterns in this population; effectiveness of multidrug-resistant organism surveillance; antimicrobial availability and access; antimicrobial prescribing practices, attitudes, and knowledge of both providers and refugees with respect to AMR; and assessment of diagnostic practices in resource-limited settings. This partially overlaps with the core elements of ASPs described by the WHO and CDC, which should also be pursued in full at the national level.²⁸ Notably, efforts toward antimicrobial stewardship in LMICs are currently underway in numerous forms, including

evaluations of hospital antibiotic stewardship programs, expansion of AMR surveillance networks, community- and education-based interventions, use of interdisciplinary teams, and international collaborations, among others.^{10,29–40} Organizations such as MSF also have numerous active projects in this space, including stewardship implementation and expansion of diagnostic capacity, as well as clinical trials, such as a recent study revealing lack of efficacy of routine antibiotic use for uncomplicated severe acute malnutrition in Niger and another recent study of the epidemiology of drug-resistant bloodstream infections in burn patients in Iraq.^{41–43} These efforts in LMICs could serve as a starting point for adaptation in the refugee population.

Considerations should also be made for differences in living situation among refugee populations. Those residing in congregate settings such as camps, such as the Rohingya in Cox's Bazar,⁴⁴ may have fluctuating population totals and may be subject to geopolitical instability. Conflict regions, such as certain Arab countries, particularly exacerbate the problem for both refugees and home populations alike.⁴⁵ Heavy metal use is an additional factor contributing to AMR that is not readily addressed by stewardship programs.⁴⁶ Even those refugees resettled in urban centers in more stable host countries may face their own challenges in integration.⁴⁷

Much work remains to be done in integrating ASPs in healthcare settings around the world. This issue is especially critical in refugee populations. Although they have garnered an increasing amount of literature in recent years,⁴⁸ including documentation of increased AMR prevalence, little attention has been given to the implementation challenges in such settings. Preliminary published data and lessons learned from WASH and infection prevention and control efforts should guide future agenda setting. Technical guidance from the United Nations Refugee Agency (UNHCR) offers direction on a range of infection prevention and control topics, including disinfection and sterilization as well as COVID-19 WASH efforts.^{49,50} Creating similar and complementary evidence-based ASP guidance for practitioners is critical to moving the global AMR agenda forward.

Recent events, such as the withdrawal of United States military forces from Afghanistan and the arrival of Haitian asylum seekers at the United States southern border in the wake of the Haitian earthquake and presidential assassination further highlight the geopolitical volatility that places these populations at high risk. These populations already show higher prevalence rates of multidrug-resistant organism carriage.^{1–5} Without such targeted efforts, progress of refugee health efforts will stall, risking loss of the progress of ASP efforts not only in this population but in LMICs worldwide.

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