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Health Care–Acquired Infections in Low- and Middle-Income Countries and the Role of Infection Prevention and Control



Gina Maki, DO^{a,*}, Marcus Zervos, MD^b

KEYWORDS

• Hospital infections • Infection control • Antibiotic resistance • LMIC

KEY POINTS

- Health care–associated infections (HAIs) are a large cause of morbidity worldwide.
- Low- and middle-income countries have larger burdens of HAIs than high-income countries.
- Infection prevention and control plays a large role in decreasing the rate of HAIs and reducing antimicrobial resistance.

INTRODUCTION

Health care–associated infections (HAIs) account for many morbidity and mortality worldwide.¹ There are hundreds of millions of people affected by HAIs in all countries worldwide each year; however, low- and middle-income countries (LMIC) are disproportionately affected in adverse outcomes.² The total burden of HAIs is unknown especially in LMIC due to a lack of reported data, with LMIC studies reporting HAIs often being from individual centers or wards.³ HAIs are infections that begin 48 hours or more after hospitalization or within 30 days after receiving health care.¹ Infection prevention and control (IPC) programs have been instituted in many settings in effort to decrease HAIs. They have the goal to reduce the risk of HAIs between patients, health care workers (HCW), and the environment, leading to a reduction in HAI-related morbidity, mortality, and avoidable costs.² Because of limited resources, LMIC face significant and often insurmountable challenges to accomplish this goal.

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Therefore, optimal approaches must be tailored for LMIC and balance the feasibility, effectiveness, and cost.

RISK FACTORS TO ACQUIRE HEALTH CARE–ASSOCIATED INFECTIONS IN LOW- AND MIDDLE-INCOME COUNTRIES

Common types of HAI include central line–associated bloodstream infections (CLABSI), catheter-associated urinary tract infections, surgical site infections, hospital-acquired pneumonia, ventilator-associated pneumonia (VAP), clostridium difficile infections, and multidrug-resistant organisms (MDRO). Individual and system factors can contribute to the acquisition of HAIs, including increased length of health care facility stay, use of invasive devices, older patient age, patient comorbidities, mechanical ventilatory support, and stay in intensive care unit.⁴ LMIC have additional risk factors contributing to HAI acquisition such as lack of resources and surveillance systems, lack of personnel and understaffing, lack of education in IPC and HAIs, overcrowding, and lack of supplies including cleaning supplies and soaps.

SURVEILLANCE AND RATES OF HEALTH CARE–ASSOCIATED INFECTIONS

Surveillance plays an important role in addressing rates of HAIs. By surveilling and monitoring specific HAIs problem areas can be identified; furthermore, gathering initial data and continued monitoring can assess areas of improvement and areas that continue to require improvement after program implementation. A study in India revealed an infection rate of 33 infections per 100 patients.⁵ The most common HAIs in this study were urinary tract infections, followed by surgical site infections, wound infections, and nosocomial pneumonia.⁵ A meta-analysis reviewing HAIs in Ethiopia reviewed 18 studies with 13,821 patients. This study found the pooled prevalence of HAIs among these studies to be 17.0%. The highest rates of HAIs were found to be surgical site infections, followed by urinary tract infections, bloodstream infections, then respiratory tract infections.⁶

How surveillance can be performed in low-resource settings should be addressed when starting a program within a facility.⁷ Prospective clinical surveillance is often too resource intensive for low-resource settings. Automated surveillance is another recommended form for HAI surveillance that can also be difficult for resource-limited settings.⁸ A study in South Africa looked at 3 various techniques including antimicrobial prescription surveillance, laboratory surveillance, and repeated point prevalence surveys. They found that the repeated point prevalence surveys were significantly less sensitive than the antimicrobial prescription and laboratory surveillance. Both laboratory and prescription-based surveillance had risk of false-positive identification of HAIs. The combination of antimicrobial prescription with laboratory surveillance reduced the false-positive rate. This combination also improved the estimates of HAI incidence, suggesting that this combination of surveillance may provide the most accurate estimate of the true HAI burden.⁹ These methods can be considered as an alternative to more resource-intensive methods in resource-constrained settings. Although LMIC often face many challenges including limited human resources, diagnostics, and medical supplies, it is important to work around these barriers to find ways to best implement HAI surveillance.^{10,11}

ANTIMICROBIAL RESISTANCE SURVEILLANCE

With an increase in MDRO and the limited antimicrobials to treat the many new resistant infections that are in circulation, it is important to be able to monitor the rates of

antimicrobial resistance (AMR). Many MDRO originate in LMIC where the ability to control the spread can be limited due to a lack of resources. A major concern for AMR bacteria are the highly resistant carbapenemases. Two major examples are *Klebsiella pneumoniae* carbapenemase, which was identified in 2001, and New Delhi metallo- β -lactamase-1, identified in 2008^{12,13}—2 highly resistant carbapenemases that have since been found to spread worldwide.^{14,15}

Many health care facilities in LMIC lack the infrastructure and financial and human resources to create a robust program for AMR surveillance. With increasing resistance and the rapid spread among and between countries, it is of the utmost importance to monitor AMR.

In hospitals that are able to assess AMR, there are reports of high levels of HAI infections.⁵ A study in India revealed a large percentage of nosocomial infections, with a high rate of resistance. More than 80% of isolates were gram-negative bacteria; common organisms isolated were *Pseudomonas aeruginosa*, *Escherichia coli*, *Acinetobacter baumannii*, as well as the gram-positive *Staphylococcus aureus*. Of these isolates, 69.9% of isolates were resistant to all antibiotics for which susceptibility testing was performed. *S aureus* isolates were found to be resistant to methicillin in 71.4% of isolates, and 88.2% were found to be sensitive to vancomycin, showing the concern for increasing glycopeptide resistance.⁵ Another study in India revealed the most common organisms in VAP to be gram-negative organisms, with the most frequently isolated being *Acinetobacter* spp., followed by *Klebsiella* spp. and *Pseudomonas* spp.¹⁶ In this study, 23% of the isolates causing VAP were multidrug resistant.

ANTIMICROBIAL STEWARDSHIP IN RELATION WITH INFECTION PREVENTION AND CONTROL

By the year 2050, global estimates of the impact of AMR will include more than 10 million annual deaths, making AMR the leading cause of death worldwide, surpassing deaths due to cancer, diabetes, and diarrheal diseases.¹⁷ With limited antibiotics continuing to be produced as the rates of AMR increase, prevention plays a key role in tackling this major issue. Antimicrobial usage has seen exponential increase in LMIC over the last decade. The increase in antimicrobial use has been enabled by increasing incomes, availability of cheaper generic antimicrobials, unregulated over-the-counter pharmacy dispensation, indiscriminate antimicrobial use in livestock, and inappropriate antimicrobial use in health care; this is further aggravated by inadequate public health and infection control measures. Unfortunately, increased antimicrobial consumption has exerted selective pressure leading to emergence of resistant organisms. Because antimicrobial consumption is the driving factor for AMR, there needs to be a coordinated effort to optimize antimicrobial usage and prevent the transmission of resistant organisms. AMR poses a grave threat to the potential gain achieved in reducing mortality related to infections in the previous century by rendering all available antimicrobials ineffective against the resistant organisms. Because there are no newer antimicrobials in the pipeline for the foreseeable future, antimicrobial stewardship (AMS) programs have emerged as a key strategy in combating AMR. Both AMS and IPC programs are important in limiting the development and spread of MDRO.

In September 2016, the United Nations General Assembly held the first ever high-level meeting regarding AMR. The emphasis of the meeting focused on taking a One Health approach, recognizing the relation of health among humans, animals, and the environment. In response to this, many countries developed a national action plan for combating AMR. Although many countries developed a national action plan,

few had started the process of program implementation to address AMR. The World Health Organization (WHO) created a practical toolkit for AMS programs in health care facilities in LMIC.¹⁸ This toolkit was created to address the fourth strategic objective of the global action plan on AMR¹⁹ by giving guidance on how to develop AMS programs or to strengthen programs that are already in place, including IPC programs. The toolkit begins with a checklist to be reviewed by the national leadership, hospital leadership, and hospital staff. This lends a point to begin assessment of what is in place and what the next steps are. The importance of the link between IPC and AMS is evident throughout the document when discussing the prevention of developing and spreading of AMR. Both programs have a goal of improving patient outcomes and patient safety and are used in the prevention of MDRO infections. In 2017 the Geneva IPC-think tank brought together 42 international experts to discuss strengthening of the global IPC network with the outcome of recognizing the importance of combining AMS and IPC under one umbrella.²⁰

HEALTH CARE-ASSOCIATED TUBERCULOSIS

In 2018 there were an estimated 10 million new cases of tuberculosis (TB) worldwide, with 1.5 million TB deaths.²¹ HCW remain at risk for contracting TB in the health care setting.²² Risk seems particularly high when there is increased exposure combined with inadequate facilities for respiratory isolation and lack of rapid diagnostic tools.^{23,24} In a review comparing the risk of TB infection and disease in high-income countries (HIC) and LMIC, the median prevalence of latent TB infection in HCW was 63% in LMIC and 24% in HIC.²⁴ The median annual incidence of TB infection that was considered to be caused by health care exposure was 5.8% in LMIC and 1.1% in the HIC studied.

The WHO guidelines recommend a prioritization of administrative controls as the most important measures, because engineering and personal controls do not work in the absence of solid administrative measures. Although engineering measures require resources, opening windows to increase natural ventilation and the use of fans to control the direction of airflow are examples of inexpensive measures that can be implemented. Personal measures are the most expensive and least effective measures and, therefore, should only be used in specialized settings and when all other IPC measures have been implemented.²⁵

EMERGING INFECTIONS: CORONAVIRUS DISEASE 2019

The coronavirus disease 2019 (COVID-19) caused by the novel severe acute respiratory syndrome coronavirus (SARS-CoV-2) was declared a pandemic by the WHO on March 11, 2020. It has been important to note the nature of asymptomatic spread of the virus. Many of those infected with the SARS-CoV-2 do not develop symptoms, and in those that do become symptomatic there is a period of transmissibility before the onset of symptom development.^{26,27}

COVID-19 has been found to affect certain vulnerable populations, which require additional focus and precautions. Many of the vulnerable populations that have been noted to be heavily affected in HIC make up much of the populations of LMIC. Indigenous populations often live outside of the large urban centers with limited access to medical care as well as may have language barriers and beliefs, which can lead to difficulties in seeking and obtaining medical care.²⁸ Many LMIC health care facilities function with an already limited supply of resources, which can be exacerbated by the pandemic. The workload of HCWs is increased by the pandemic, as there is often already limited human resources. Living in close quarters is a risk for increased

transmission, and it is known that often large families that are financially limited live in poor housing conditions.²⁸ The elderly have been shown to have the highest risk of poor outcomes with COVID-19 infection. Nursing home residents were heavily affected by the COVID-19 pandemic, with multiple cities reporting outbreaks within the nursing homes.²⁹ In one study of nursing homes in Detroit, Michigan, USA, it was found that there was a 44% COVID-19 attack rate among the nursing home residents, with 37% of those requiring hospitalizations, and 24% died.³⁰ Another vulnerable population noted in the United States were nonwhite Americans, especially Black Americans. In Michigan, Black Americans make up 14% of the population; however, they made up 37% of COVID-19 cases and 42% of deaths.^{31,32} It is important to be aware of these vulnerable populations in order to address prevention of adverse outcomes.

COVID-19 has played a role in the contribution to HAIs and AMR.^{29,33} Multiple studies revealed the extensive use of antibiotic coverage in COVID-19 pneumonia despite the low evidence of confirmed bacterial coinfection.^{34–36} This evidence shows the opportunity for AMS efforts to decrease the overuse of antimicrobials in COVID-19 infection. With COVID-19 hospital admissions comes increased hospital stays and increased duration of stay, which in turn leads to an increased risk for acquiring HAIs. Early in the pandemic, personal protective equipment became high in demand, and many settings worldwide developed a severe shortage. With a shortage in personal protective equipment, this decreased the comfort of HCW entering COVID-19 patient rooms and/or areas, which led to less time spent at the bedside, which in turn led to a decrease in infection prevention care, such as addressing of ventilator and lines bundles. With increased availability of personal protective equipment and increased learning of the disease, the comfort of caring for patients with COVID-19 disease increases and more attention can be paid to the details of prevention of HAIs.

Wearing masks was an early recommendation to stop the spread of the COVID-19 infection.³⁷ It is important for all people to wear a mask and not only COVID-19-positive patients due to the asymptomatic transmission of the virus. For HCWs working with COVID-19 positive and suspected patients, it was recommended to use both droplet and contact precautions, with the use of a mask, with N-95 or respirator use in the setting of an aerosol generating procedure, along with gown, gloves, and eye protection.³⁷

During the COVID-19 outbreak the WHO created guidance that included IPC recommendations to implement strategies with the goal of preventing or limiting health care transmission of COVID-19.³⁸ These included ensuring triage, early recognition, and source control; applying standard precautions for all patients; implementing additional precautions such as droplet, contact, and airborne when applicable; implementing administrative controls; and using environmental and engineering controls.³⁸ Within this guidance, they reinforced the recommendation of standard precautions in all patients at all times within health care facilities (**Box 1**).^{38–40} These practices can also inhibit the spread of other HAIs.

Recommended isolation precautions can be a challenge in LMIC settings. In addition to standard precautions as described earlier, contact and droplet precautions in all suspected or confirmed COVID-19 cases are recommended.³⁸ These recommendations include wearing a medical mask, eye protection such as goggles or a face shield, gown, and gloves when possible. Additional precautions can be implemented when feasible including cohorting, separation of patients by 1 m apart, and airborne precautions for aerosol-generating procedures such as tracheal intubation and noninvasive ventilation.

Box 1

Standard precautions for all patients

1. Hand hygiene
 - a. Cleanse hands with an alcohol-based hand rub or with soap and water;
 - b. Alcohol-based hand rubs are preferred if hands are not visibly soiled;
 - c. Wash hands with soap and water when they are visibly soiled.
2. Respiratory hygiene
 - a. Cover nose and mouth with a tissue or elbow when coughing or sneezing;
 - b. Offer a medical mask to patients with suspected COVID-19 while they are in waiting/public areas or in cohorting rooms;
 - c. Perform hand hygiene after contact with respiratory secretions.
3. Correct personal protective equipment according to risk
 - a. Maintain adequate and regular supplies;
 - b. Maintain staff training.
4. Safe injection practices, sharps management and injury prevention
 - a. Using a clean workspace;
 - b. Hand hygiene before and after;
 - c. Use a sterile safety-engineered syringe;
 - d. Use sterile vial of medication and diluent;
 - e. Appropriate skin cleaning and antisepsis;
 - f. Appropriate collection of sharps;
 - g. Appropriate waste management.
5. Safe handling, cleaning, and disinfection of patient care equipment
 - a. Clean patient care equipment between each patient use.
6. Appropriate environmental cleaning; safe handling and cleaning of soiled linen
 - a. Clean and soiled linen should be stored and handled separately;
 - b. Cleaning should occur on regular basis per standard protocols.
7. Appropriate waste management
 - a. Ensure appropriate waste management protocols are followed.

Data from Refs. ^{38–40}

HEALTH AND ECONOMIC IMPACT

The cost of health care is an important factor for all problems and interventions in the health care setting. Associated factors such as prolonged hospital stay, disability, increased AMR, increased costs, and increased deaths are more pronounced in LMIC. VAP is a leading cause of HAI in patients within the intensive care unit. VAP has been found to occur at a higher rate in Asian countries than averages from the International Nosocomial Infection Control Consortium data.⁴¹ The International Nosocomial Infection Control Consortium reported that device-associated infections increase length of stay by 10 days, costs between \$5000 and \$12,000 US dollars, and doubles the rate of mortality.^{42–44} In LMIC, although the magnitude and impact of the problem is more remarkable, there are few objective data on the financial burden, and this burden varies from country to country.^{43,44} The limitations in health care facilities, including infrastructure, patient load, and staff shortages, provide many challenges. Limitations in access to care, issues of sanitation, and poverty also complicate measures to control HAIs.

EXAMPLE OF SUCCESSFUL INFECTION CONTROL STRATEGY IN RESOURCE-LIMITED SETTINGS

The International Nosocomial Infection Control Consortium implemented a multidimensional approach on VAP in 11 hospitals in Argentina over a 4-year period. The

baseline data of this study revealed that there were higher rates of VAP per 1000 mechanically ventilated days when compared with HIC including USA VAP rates from the Centers for Disease Control and Prevention and German data from the German Krankenhaus Infektions Surveillance System. Through interventions including a bundle of infection prevention practice interventions, education, outcome surveillance, process surveillance, feedback on VAP rates and consequences, and performance feedback of process surveillance there was a 52% rate reduction in VAP.⁴⁵ They found that for each VAP there was an extra length of stay of 16 days on average, 4-fold higher than patients without VAP, with a cost of \$1000 US dollars per each bed-day; this led to a total savings of 176 days per each intensive care unit per year and a savings of \$176,000 US dollars per year.

A consortium of 15 LMIC developed a successful strategy by focusing on education, performance feedback and outcome, and outcome and process surveillance. The study took place in 86 intensive care units and showed improved IPC adherence and reduced CLABSI incidence by 33% in the first 6 months of the program and by 54% over the first 24 months.⁴⁶ The number of deaths in patients with CLABSI decreased by 58%. Specific interventions in which improvement was noted included adherence to hand hygiene, use of maximal sterile barriers during line insertion, use of chlorhexidine for antiseptic measures, removal of unneeded catheters, and decreased duration of catheters.⁴⁶

These studies reveal that with bundled IPC practices the rates of HAIs such as VAP and CLABSI can be drastically reduced.

DESIGNING AND SUSTAINING INFECTION CONTROL PROGRAMS AND INTERVENTIONS

Once the assessment of the need for IPC programs is evaluated, it is important to then address the implementation. It was noted by the WHO that implementation of the measures to address IPC and AMR are often the largest challenge. They recommend that in the development of any IPC or AMS curriculum implementation skills should be a priority.⁴⁷ A manual was published in 2017 by the WHO in an effort to be a practical manual to support the implementation of WHO guidelines on the core components of IPC programs with a focus on low-resource settings. The 3 aims of the manual include the following:

“(1) to provide clear direction and supporting resources to aid the development of a practical outcome-focused action plan, (2) to describe how to operationalize the plan based on evidence and national-level implementation experience informed by local examples and existing realities, and (3) to support sustainability of the plan with a focus on integrating and embedding IPC within relevant national policies and strategies.”⁴⁸

According to the WHO manual there are 8 core components relevant to the facility-level IPC programs, outlined in **Box 2**.

For those with an IPC program already started, it is important to also evaluate for sustainability and improvement. In the WHO guide for IPC, they recommend a 5-step approach for IPC program improvement (**Box 3**) with more in-depth guidance within the manual.⁴⁹

CREATING AN ANTIMICROBIAL STEWARDSHIP PROGRAM

As AMS programs play a large role in the limiting of development of AMR and MDROs, it is important for health care facilities to develop an AMS program that is adjusted to fit within the current needs and resources. WHO created a toolkit that serves as a document describing how to begin and build a successful AMS

Box 2

Core components relevant to the facility-level infection prevention and control program

1. IPC programs
2. Evidence-based guidelines
3. Education and training
4. Health care–associated infection surveillance
5. Multimodal strategies
6. Monitoring and audit of IPC practices and feedback
7. Workload, staffing and bed occupancy
8. Built environment, materials, and equipment for IPC

Data from World Health Organization. Improving infection prevention and control at the health facility: Interim practical manual supporting implementation of the WHO Guidelines on Core Components of Infection Prevention and Control Programmes. Geneva: World Health Organization; 2018.(WHO/HIS/SDS/2018.10).

program within health care facilities in LMIC.¹⁸ In creation of the toolkit, interviews were undertaken in order to evaluate the feasibility of the toolkit within LMIC.⁵⁰ Input was gathered from national leaders, health care facility leadership, and health care facility staff. This input was then incorporated into the toolkit to ensure the most

Box 3

Core components relevant to the facility-level infection prevention and control program

Step 1. Preparing for action: this step ensures that all of the prerequisites that need to be in place for success are addressed, including the necessary resources (human and financial), infrastructures, planning and coordination of activities, and the identification of roles and responsibilities (including key opinion leaders and champions). The facility senior managers/ leaders play a critical role in this step.

Step 2. Baseline assessment: conducting an exploratory baseline assessment of the current situation, including the identification of existing strengths and weaknesses, is critical for developing a tailor-made action plan that addresses the reality of a health care facility. A ready-to-use assessment tool based on the WHO IPC core components is available for step 2 (WHO IPC Assessment Framework [IPCAF]). Ideally, additional IPC assessment tools (eg, the Hand Hygiene Self-assessment Framework [HHSAF] and/or observation-based tools to evaluate IPC practices) could be used.

Step 3. Developing and executing an action plan: the results of the baseline assessment support the development and execution of an action plan based around a multimodal improvement strategy.

Step 4. Assessing impact: conducting a follow-up assessment using the same tools as in step 2 is crucial to determine the effectiveness of the plan. The focus is on impact, acceptability, and cost-effectiveness.

Step 5. Sustaining the program over the long term: an important step in the cycle of improvement is to develop an ongoing action plan and review schedule to support the long-term impact and benefits of the IPC program, thus contributing to its overall impact and sustainability.

Data from World Health Organization. Improving infection prevention and control at the health facility: Interim practical manual supporting implementation of the WHO Guidelines on Core Components of Infection Prevention and Control Programmes. Geneva: World Health Organization; 2018 (WHO/HIS/SDS/2018.10).

usability. The WHO AMS toolkit is divided into 6 sections: (1) Structural Core Elements for AMS Implementation at the National Level; (2) Structural Core Elements for AMS Implementation at the Facility Level; (3) Planning AMS Programs; (4) Performing AMS Interventions; (5) Assessing AMS Programs; and (6) Education and Training. During the feasibility studies of the WHO AMS toolkit, it was noted that strong leadership support at the national and senior facility management levels was needed for successful implementation.⁵⁰ The WHO AMS toolkit is a resource for facilities within LMIC to create a strong AMS program and serves as a reference to continue to build on structures put in place, such as current IPC committees, in an effort to continue to control the development and spread of AMR.¹⁸

ADDRESSING GAPS WHILE PRIORITIZING RESOURCES

To prioritize resources, efforts should first focus on inexpensive yet high-impact IPC measures in order to increase success with limited resources and then later medium-term and long-term solutions. Low-cost measures, such as educational programs on hand hygiene and prevention of device-associated infections, have shown cost-effectiveness and should be the first items to be addressed. When considering IPC measures that are applicable to the setting and resources, it is best to first consider the available national guidelines or international guidelines that address the LMIC settings and resources. Examples are the WHO guidelines for injection safety,⁵¹ hand hygiene,⁵² and for the prevention of TB in health care facilities in resource-limited settings²⁵ or the use of checklists, such as the surgical safety checklist, to reduce morbidity and mortality in a global population.⁵³ Guidelines, recommendations, and interventions known to be effective in HIC settings can be a starting point to prioritize and plan how and where measures should be implemented.

SUMMARY

IPC programs are an important tool in the prevention of HAIs. In order to be practical, measures for IPC programs should be simple, cost-effective, and designed to suit the local needs and circumstances. Evidence-based measures should be used, along with achievable goals and a plan for short-term, medium-term, and long-term actions. More studies are necessary to evaluate the implementation of programs and policies that are possible in LMIC. HIC must have a shared interest in developing the capacity of neighboring countries and can serve an important role by providing training and resources.

As the health care environment continues to change, new challenges and risks arise for HAIs. It is important for continued education and awareness, as well as political engagement in the support of IPC programs to halt the progression of HAIs.

CLINIC CARE POINTS

- When developing infection control practices in a low resource setting, use a stepwise approach based on available resources.
- Strategies must start with simple and cost-effective measures and then expand to include more complicated measures.
- It is important to have administrative leadership input when developing infection control and antimicrobial stewardship programs.

DISCLOSURE

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